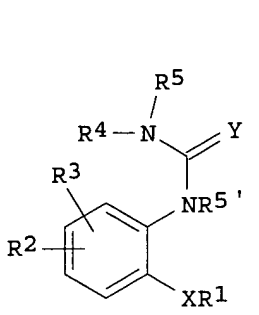
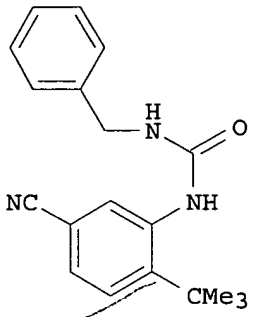
4 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I



II

AB Title compds. I [X = single bond, O, CO, S, NH, or alkylimino; Y = O, S, or NCN; R1 = alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R2 = H, alkyl, haloalkyl, alkenyl, alkynyl, cyano, NO2, CHO, CO2H, halo, (un)substituted amino, etc.; R3 = H, alkyl, OH, alkoxy, (un)substituted amino, cyano, NO2; R4 = aryl, aralkyl, heterocyclo, heterocycloalkyl; R5, R5' = H, alkyl, (un)substituted alkylamino, haloalkyl; or R4R5 form ring with 5 to 7 members and optional O, S, or (un)substituted NH] and salts are claimed, along with 18 specific compds. which were also prepd. These compds. have potassium channel activating activity and are useful, e.g., as cardiovascular agents (no data). For example, tert-butylbenzene underwent 2,4-dinitration (70%), redn. of the 4-nitro group to amino (86%), diazotization and cyanation of the group to give a benzonitrile (42%), and redn. of the remaining nitro group with SnCl2 (100%) to give 3-amino-4-(tert-butyl)benzonitrile. Reaction of this with benzyl isocyanate gave title compd. II in 70% yield.

AN 1995:733459 CAPLUS
DN 123:143653
TI Biaryl ureas and related compounds for use as cardiovascular agents.
IN Atwal, Karnail; Ferrara, Francis N.; Ding, Charles Z.
PA USA
SO Can. Pat. Appl., 39 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

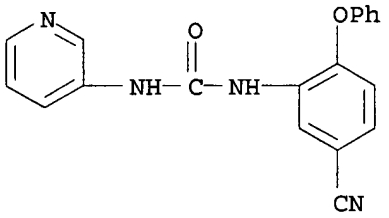
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | CA 2132771 | AA | 19950408 | CA 1994-2132771 | 19940923 |
| | US 5547966 | A | 19960820 | US 1993-134195 | 19931007 |
| | EP 656350 | A1 | 19950607 | EP 1994-306813 | 19940916 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | AU 9474463 | A1 | 19950427 | AU 1994-74463 | 19941006 |
| | AU 690133 | B2 | 19980423 | | |
| | JP 07188151 | A2 | 19950725 | JP 1994-243895 | 19941007 |
| PRAI | US 1993-134195 | | 19931007 | | |

OS MARPAT 123:143653
IT **166263-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biaryl ureas and analogs as cardiovascular agents)

RN 166263-16-7 CAPLUS

CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Z = O, S; R1 = alkyl, alkenyl, alkoxy, etc.; R2-R6 = alkyl, alkenyl, alkoxy, etc.; adjacent pair of R2-R6 together with the carbon atoms to which they are attached form (un)substituted carbocyclyl, heterocyclyl; R7 = alkyl, alkenyl, alkoxy, etc.; n = 0-3] and their pharmaceutically acceptable salts which are non-peptide antagonists of human orexin receptors, in particular orexin-1 receptors, were prepd. E.g., treatment of 4-amino-2-methylquinoline with carbonyl diimidazole in CH2Cl2 followed by addn. of 6-amino-2-methylbenzoxazole afforded II which showed pKb > 6.0 against orexin-1 receptor. In particular, compds. I are of potential use in the treatment of obesity including obesity obsd. in Type 2(non-insulin-dependent) diabetes patients and/or sleep disorders.

AN 2000:573791 CAPLUS
DN 133:164009
TI Preparation of phenyl ureas and thioureas as orexin receptor antagonists
IN Coulton, Steven; Johns, Amanda; Porter, Roderick Alan
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000047577 | A1 | 20000817 | WO 2000-EP1150 | 20000210 |
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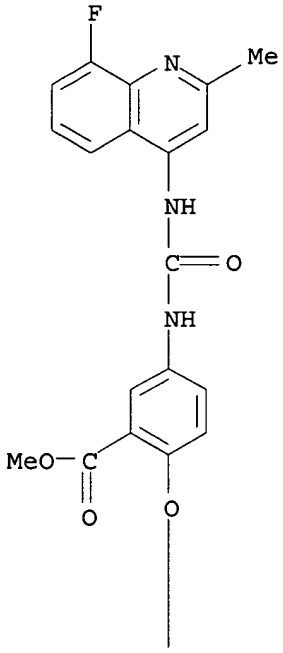
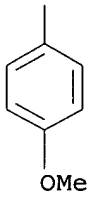
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1150977 | A1 | 20011107 | EP 2000-906324 | 20000210 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI GB 1999-3266 | A | 19990212 | | |
| GB 1999-26430 | A | 19991108 | | |
| WO 2000-EP1150 | W | 20000210 | | |

OS MARPAT 133:164009
IT **288151-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of Ph ureas and thioureas as orexin receptor antagonists)
RN 288151-08-6 CAPLUS
CN Benzoic acid, 5-[[[(8-fluoro-2-methyl-4-quinolinyl)amino]carbonyl]amino]-2-(4-methoxyphenoxy)-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A




RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

Print selected from Online session09/09/2002

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L3            8 S L2

     FILE 'CAPLUS' ENTERED AT 16:37:54 ON 09 SEP 2002
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L5            0 S L4  NOT L3

=> s l4 not l3
            26 L2
L6            0 L4 NOT L3

=> d abs bib fhitstr l4 1-26

L4   ANSWER 1 OF 26  CAPLUS  COPYRIGHT 2002 ACS
GI
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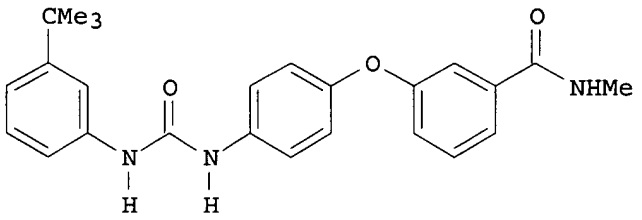


II

```
AB   Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3,
     2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl,
     2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl,
     -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were
     prepd.  Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (prepn. given) was condensed with
     3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compd. II.  Data for biol.
     activity of title compds. were given.
AN   2002:615574  CAPLUS
TI   Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase
     inhibitors
IN   Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert
     N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger,
     Timothy B.; Scott, William J.; Smith, Roger A.
PA   Bayer Corporation, USA
SO   PCT Int. Appl., 125 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2002062763      A2   20020815       WO 2002-US203361 20020207
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
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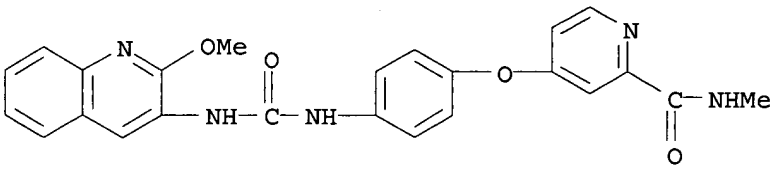
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2001-777920 A 20010207
IT **432050-22-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)
RN 432050-22-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



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 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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COST IN U.S. DOLLARS

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DICTIONARY FILE UPDATES: 8 SEP 2002 HIGHEST RN 448182-31-8

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http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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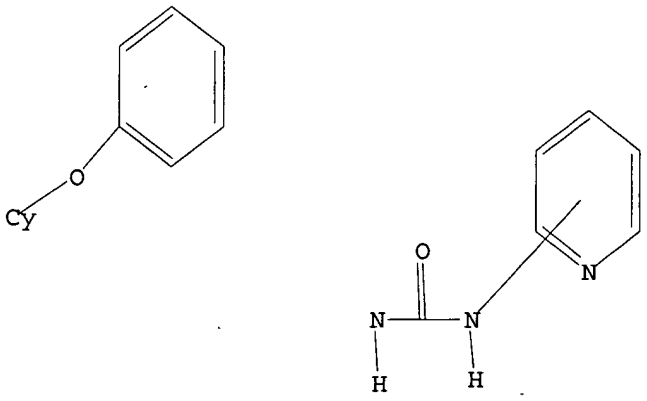


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CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

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CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

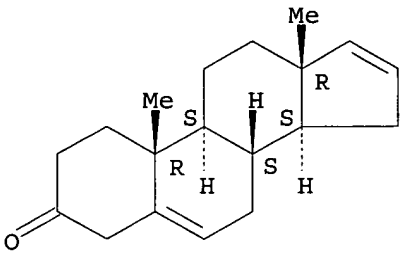
=> s l2
L3 8 L2

=> d abs bib hitstr 1-8

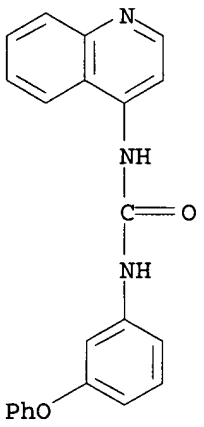
L3 ANSWER 1 OF 8 USPATFULL
AB Phenyl urea and phenylthiourea derivatives, processes for their production and their uses as pharmaceuticals are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:152635 USPATFULL
TI Phenyl urea and phenyl thiourea derivatives as HFGAN72 antagonists
IN Chan, George, Wynnewood, PA, United States
Johns, Amanda, Bishop's Stortford, UNITED KINGDOM
Jurewicz, Anthony, Royersford, PA, United States
Porter, Roderick Alan, Ashwell, UNITED KINGDOM
Widdowson, Katherine, King of Prussia, PA, United States
PA SmithKline Beecham p.l.c., Brentford, UNITED KINGDOM (non-U.S. corporation)
PI US 6410529 B1 20020625
WO 9909024 19990225
AI US 2000-485623 20000510 (9)
WO 1998-GB2437 19980813
20000510 PCT 371 date
PRAI GB 1997-17178 19970814
GB 1998-7756 19980408
DT Utility
FS GRANTED
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Sieburth, Kathryn, McCarthy, Mary E., Kinzig, Charles M.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2275
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **103614-70-6P**, Androsta-5,16-dien-3-one
(steroids as neurochem. stimulators of the VNO to alleviate pain)
RN 103614-70-6 USPATFULL
CN Androsta-5,16-dien-3-one (9CI) (CA INDEX NAME)

Absolute stereochemistry.




IT **220844-29-1P**
(prepn. of quinolinylureas and related compds. as HFGAN72 antagonists)
RN 220844-29-1 USPATFULL
CN Urea, N-(3-phenoxyphenyl)-N'-4-quinolinyl-, monohydrochloride (9CI) (CA INDEX NAME)

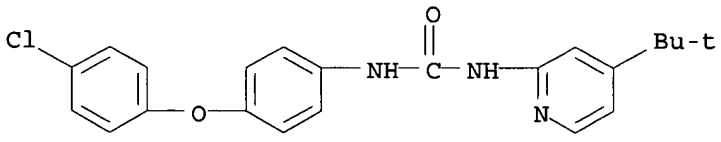



● HCl

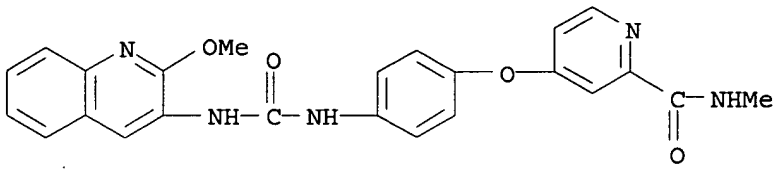
L3 ANSWER 2 OF 8 USPATFULL
AB This invention relates to the use of a group of heteroaryl ureas containing nitrogen in treating p38 mediated diseases, and pharmaceutical compositions for use in such therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:126779 USPATFULL
TI Heteroaryl ureas containing nitrogen hetero-atoms as p38 kinase inhibitors
IN Dumas, Jacques, Orange, CT, UNITED STATES
Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF
Khire, Uday, Hamden, CT, UNITED STATES
Sibley, Robert N., North Haven, CT, UNITED STATES
Hatoum-Mokdad, Holia, Hamden, CT, UNITED STATES
Monahan, Mary-Katherine, Hamden, CT, UNITED STATES
Gunn, David E., Hamden, CT, UNITED STATES
Lowinger, Timotthy B., Nishinomiya City, JAPAN
Scott, William J., Guilford, CT, UNITED STATES

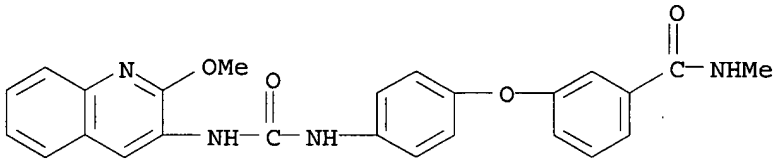
Smith, Roger A., Madison, CT, UNITED STATES
Wood, Jill E., Hamden, CT, UNITED STATES
PA BAYER CORPORATION (U.S. corporation)
PI US 2002065296 A1 20020530
AI US 2001-838286 A1 20010420 (9)
RLI Continuation-in-part of Ser. No. US 2001-778039, filed on 7 Feb 2001, PENDING Continuation-in-part of Ser. No. US 1999-425229, filed on 22 Oct 1999, PENDING Continuation of Ser. No. US 1999-257265, filed on 25 Feb 1999, ABANDONED
PRAI US 1999-115878P 19990113 (60)
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2826
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **432050-20-9P 432050-22-1P**, N-(2-Methoxy-3-quinolinyl)-N'-[4-(2-(N-Methylcarbamyl)-4-pyridyloxy)phenyl]urea **432050-23-2P**, N-(2-Methoxy-3-quinolyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea **432050-24-3P**, N-(2-Methoxy-3-quinolyl)-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea **432050-25-4P**, N-(2-Methoxy-3-quinolyl)-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea **432050-26-5P**, N-(2-Methoxy-3-quinolyl)-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea **432050-27-6P**, N-(2-Methoxy-3-quinolyl)-N'-[4-[3-(N-isopropylcarbamoyl)phenoxy]phenyl]urea **432050-28-7P**, N-(2-Methoxy-3-quinolyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea **432050-29-8P**, N-(3-Isoquinolyl)-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea **432050-33-4P**, N-(4-tert-Butyl-2-pyridinyl)-N'-[4-(4-methoxyphenoxy)phenyl]urea **432050-41-4P**, N-(4-tert-Butyl-2-pyridyl)-N'-(4-(4-methylphenoxy)phenyl)urea **432050-42-5P**, N-(4-tert-Butyl-2-pyridyl)-N'-(4-(4-pyridyloxy)phenyl)urea **432050-45-8P 432050-48-1P 432050-52-7P**, N-(Isoquinol-3-yl)-N'-(4-(3-(methylcarbamoyl)phenoxy)phenyl)urea **432050-53-8P**
(prepn. of heteroaryl ureas contg. nitrogen hetero-atoms as p38 kinase inhibitors)
RN 432050-20-9 USPATFULL
CN Urea, N-[4-(4-chlorophenoxy)phenyl]-N'-[4-(1,1-dimethylethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



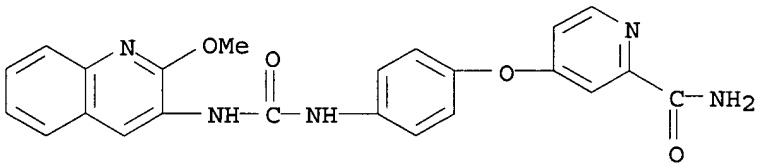

RN 432050-22-1 USPATFULL
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



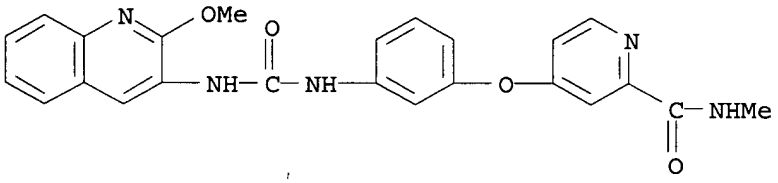
RN 432050-23-2 USPATFULL
CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



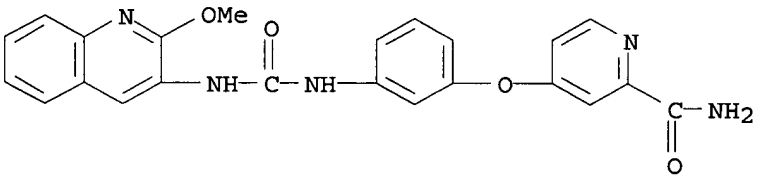
RN 432050-24-3 USPATFULL
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



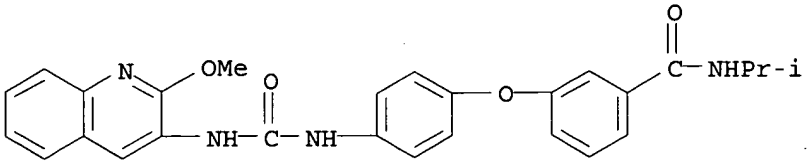
RN 432050-25-4 USPATFULL
CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



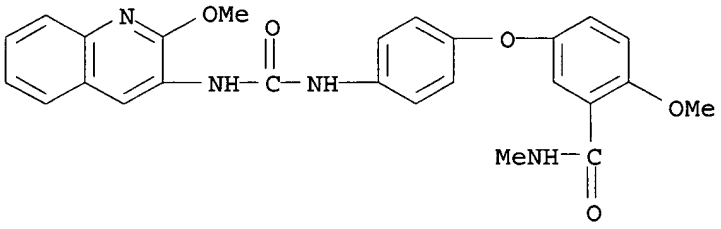
RN 432050-26-5 USPATFULL
CN 2-Pyridinecarboxamide, 4-[3-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]- (9CI) (CA INDEX NAME)



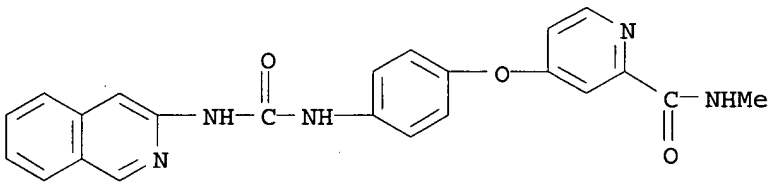
RN 432050-27-6 USPATFULL
CN Benzamide, 3-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



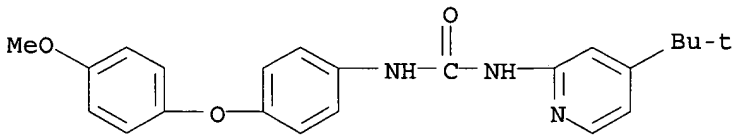
RN 432050-28-7 USPATFULL
CN Benzamide, 2-methoxy-5-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



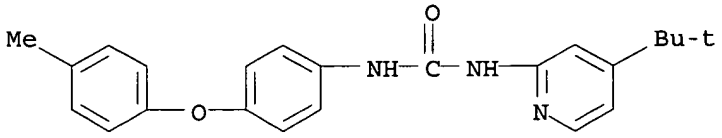
RN 432050-29-8 USPATFULL
CN 2-Pyridinecarboxamide, 4-[4-[[(3-isoquinolinylamino)carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



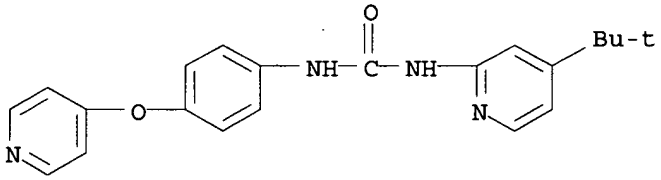
RN 432050-33-4 USPATFULL
CN Urea, N-[4-(1,1-dimethylethyl)-2-pyridinyl]-N'-[4-(4-methoxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



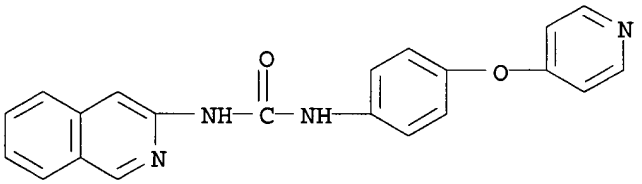
RN 432050-41-4 USPATFULL
CN Urea, N-[4-(1,1-dimethylethyl)-2-pyridinyl]-N'-[4-(4-methylphenoxy)phenyl]- (9CI) (CA INDEX NAME)



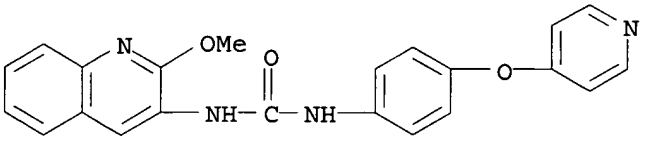
RN 432050-42-5 USPATFULL
CN Urea, N-[4-(1,1-dimethylethyl)-2-pyridinyl]-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)



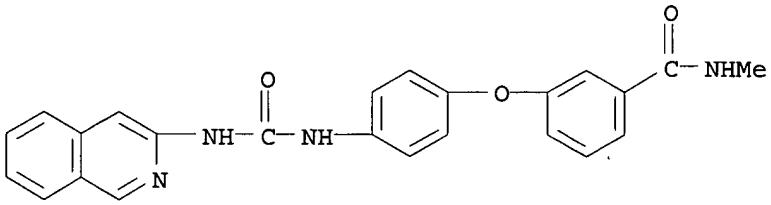
RN 432050-45-8 USPATFULL
CN Urea, N-3-isoquinolinyl-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)

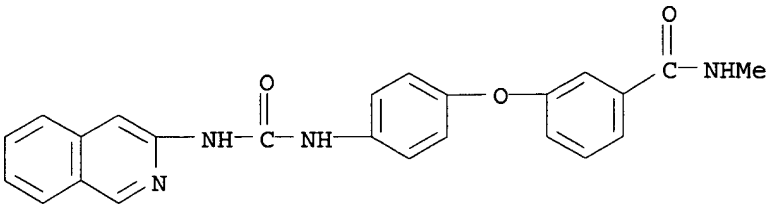


RN 432050-48-1 USPATFULL
CN Urea, N-(2-methoxy-3-quinolinyl)-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)

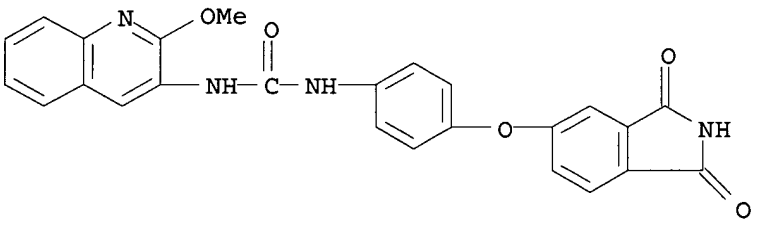


RN 432050-52-7 USPATFULL
CN Benzamide, 3-[4-[[(3-isoquinolinylamino)carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)





RN 432050-53-8 USPATFULL
CN Urea, N-[4-[(2,3-dihydro-1,3-dioxo-1H-isoindol-5-yl)oxy]phenyl]-N'-(2-methoxy-3-quinolinyl)- (9CI) (CA INDEX NAME)

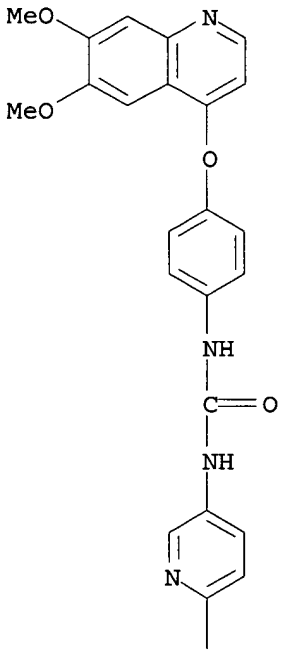


L3 ANSWER 3 OF 8 USPATFULL
AB The present invention relates to novel quinoline derivatives and quinazoline derivatives represented by the following formula (I): ##STR1## [wherein R.sub.1 and R.sub.2 are each independently H or C.sub.1 -C.sub.4 -alkyl, or R.sub.1 and R.sub.2 together form C.sub.1 -C.sub.3 -alkylene, X is O, S or CH.sub.2, W is CH or N, and Q is a substituted aryl group or substituted heteroaryl group] and their pharmaceutically acceptable salts, having platelet-derived growth factor receptor autophosphorylation inhibitory activity, to pharmaceutical compositions containing these compounds, and to methods for the treatment of diseases associated with abnormal cell growth such as tumors.

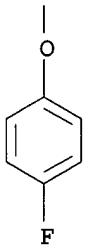
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000:150184 USPATFULL
TI Quinoline and quinazoline derivatives inhibiting platelet-derived growth factor receptor autophosphorylation and pharmaceutical compositions containing the same
IN Kubo, Kazuo, Takasaki, Japan
Ohyama, Shinichi, Takasaki, Japan
Shimizu, Toshiyuki, Takasaki, Japan
Nishitoba, Tsuyoshi, Takasaki, Japan
Kato, Shinichiro, Takasaki, Japan
Murooka, Hideko, Takasaki, Japan
Kobayashi, Yoshiko, Takasaki, Japan
PA Kirin Beer Kabushiki Kaisha, Tokyo-to, Japan (non-U.S. corporation)
PI US 6143764 20001107
WO 9717329 19970515
AI US 1998-68660 19980506 (9)
WO 1996-JP3229 19961105
19980506 PCT 371 date
19980506 PCT 102(e) date
PRAI JP 1995-313555 19951107
JP 1996-62121 19960223

DT Utility
FS Granted
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Foley & Lardner
CLMN Number of Claims: 52
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5569
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **190727-92-5P**
(prepn. of quinoline and quinazoline derivs. inhibiting platelet-derived growth factor receptor autophosphorylation)
RN 190727-92-5 USPATFULL
CN Urea, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[6-(4-fluorophenoxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A



L3 ANSWER 4 OF 8 USPATFULL

AB Compounds of general formula (1) ##STR1## are described wherein Y is a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; X is --O--, --S-- or --N(R.sup.7)--, where R.sup.7 is a hydrogen atom or an alkyl group; R.sup.2 is an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 and R.sup.4, which may be the same or different, is each a hydrogen atom or an alkyl, --CO.sub.2 R.sup.8 (where R.sup.8 is a hydrogen atom or an alkyl, aryl, or aralkyl group), --CONR.sup.9 R.sup.10 (where R.sup.9 and R.sup.10 which may be the same or different is each a hydrogen atom or an alkyl, aryl or aralkyl group), --CSNR.sup.9 R.sup.10, --CN, --CH.sub.2 CN group; Z is --(CH.sub.2).sub.n -- (where n is zero or an integer 1, 2 or 3; R.sup.5 is an optionally substituted monocyclic or bicyclic aryl group optionally containing one or more heteroatoms selected from oxygen, sulphur or nitrogen atoms; R.sup.6 is a hydrogen atom or a hydroxyl group; and the salts, solvates, hydrates, prodrugs and N-oxides thereof. Compounds according to the invention are potent and selective phosphodiesterase type IV inhibitors and are useful in the prophylaxis and treatment of diseases such as asthma where an unwanted inflammatory response or muscular spasm is present.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 1999:121385 USPATFULL

TI Trisubstituted phenyl derivatives and processes for their preparation

IN Warrellow, Graham John, Middlesex, United Kingdom HA6 3QU
Cole, Valerie Anne, Buckinghamshire, United Kingdom SL1 7NH
Alexander, Rikki Peter, Buckinghamshire, United Kingdom HP12 3HY

PA Celltech Therapeutics, Limited, Berkshire, United Kingdom (non-U.S. corporation)

PI US 5962483 19991005

AI US 1998-8173 19980116 (9)

RLI Division of Ser. No. US 1995-543962, filed on 17 Oct 1995, now patented, Pat. No. US 5739144 which is a continuation of Ser. No. US 1995-384612, filed on 2 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-208656, filed on 9 Mar 1994, now abandoned

PRAI GB 1993-4920 19930310

DT Utility

FS Granted

EXNAM Primary Examiner: Davis, Zinna Northington

LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP

CLMN Number of Claims: 20

ECL Exemplary Claim: 1

DRWN No Drawings

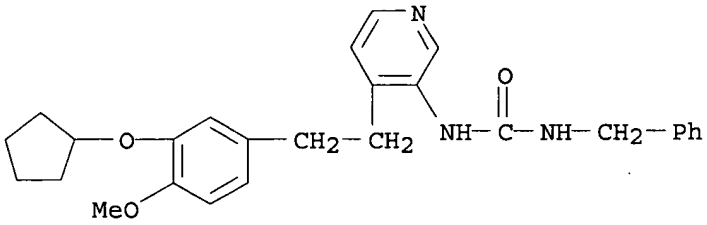
LN.CNT 1701

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **159196-19-7P**
(prepn. of heterocyclic trisubstituted Ph derivs. as phosphodiesterase inhibitors)

RN 159196-19-7 USPATFULL

CN Urea, N-[4-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethyl]-3-pyridinyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 8 USPATFULL

AB This invention is directed to the pharmaceutical use of phenyl compounds, which are linked to an aryl moiety by various linkages, for inhibiting tumor necrosis factor. The invention is also directed to the compounds, their preparation and pharmaceutical compositions containing these compounds. Furthermore, this invention is directed to the pharmaceutical use of the compounds for inhibiting cyclic AMP phosphodiesterase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 1999:92693 USPATFULL

TI Compounds containing phenyl linked to aryl or heteroaryl by an aliphatic- or heteroatom-containing linking group

IN Fenton, Garry, Dagenham, United Kingdom
Morley, Andrew David, Dagenham, United Kingdom
Palfreyman, Malcolm Norman, Dagenham, United Kingdom
Ratcliffe, Andrew James, Dagenham, United Kingdom
Sharp, Brian William, Dagenham, United Kingdom
Thurairatnam, Sukanthini, Dagenham, United Kingdom
Vacher, Bernard Yvon Jack, Dagenham, United Kingdom
Ashton, Michael John, Dagenham, United Kingdom
Cook, David Charles, Dagenham, United Kingdom
Hills, Susan Jacqueline, Dagenham, United Kingdom
McFarlane, Ian Michael, Dagenham, United Kingdom
Vicker, Nigel, Dagenham, United Kingdom

PA Rhone-Poulenc Rorer Limited, West Malling, United Kingdom (non-U.S. corporation)

PI US 5935978 19990810

AI US 1993-98178 19930728 (8)

RLI Continuation-in-part of Ser. No. WO 1992-GB153, filed on 28 Jan 1992, now abandoned

PRAI GB 1991-1777 19910128
GB 1991-17727 19910816
GB 1992-15989 19920728
GB 1992-16005 19920728
GB 1992-16006 19920728
GB 1992-16008 19920728
GB 1992-16764 19920807
GB 1993-10633 19930521
GB 1993-10938 19930527
GB 1993-11281 19930601
GB 1993-14847 19930716

DT Utility

FS Granted

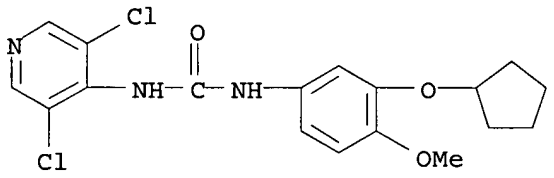
EXNAM Primary Examiner: Davis, Zinna Northington

LREP Parker, III, Raymond S., Savitzky, Martin F.

CLMN Number of Claims: 36

ECL Exemplary Claim: 1

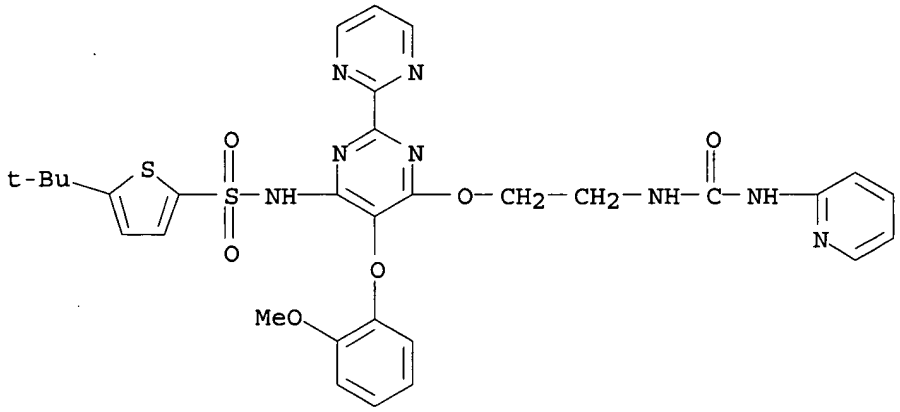
DRWN No Drawings
LN.CNT 4870
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **159782-49-7P**, N-(3,5-Dichloropyrid-4-yl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as tumor necrosis factor and c-AMP phosphodiesterase inhibitors)
RN 159782-49-7 USPATFULL
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)



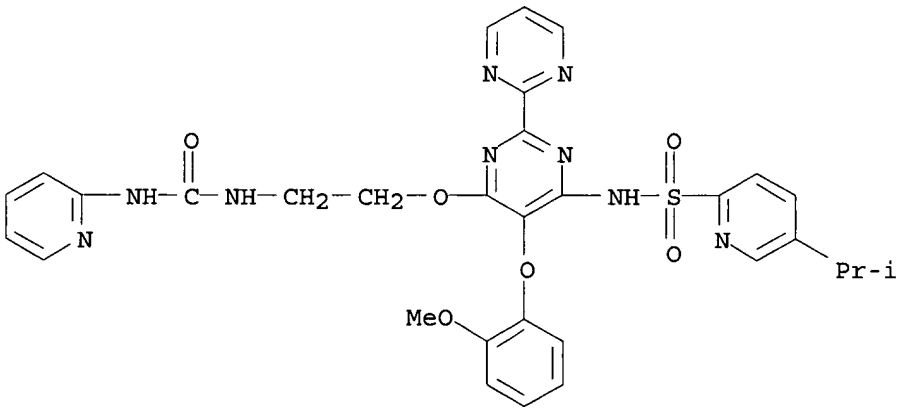

L3 ANSWER 6 OF 8 USPATFULL
AB Compounds of the formula ##STR1## wherein the variables are hereinbelow defined. The compounds of formula I are inhibitors for endothelin receptors. They can be used for the treatment of disorders which are associated with endothelin activities, especially circulatory disorders such as hypertension, ischaemia, vasospasms and angina pectoris.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:144107 USPATFULL
TI Sulphonamides
IN Breu, Volker, Schliengen, Germany, Federal Republic of
Burri, Kaspar, Binningen, Switzerland
Cassal, Jean-Marie, Mulhouse, France
Clozel, Martine, St. Louis, France
Hirth, Georges, Huningue, France
Loffler, Bernd-Michael, Oberrimsingen, Germany, Federal Republic of
Muller, Marcel, Frenkendorf, Switzerland
Neidhart, Werner, Hagenthal le Bas, France
Ramuz, Henri, Birsfelden, Switzerland
PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 5837708 19981117
AI US 1996-730422 19961015 (8)
RLI Continuation-in-part of Ser. No. US 1996-676313, filed on 18 Jul 1996
PRAI CH 1994-3559 19941125
WO 1995-CH131 19950606
DT Utility
FS Granted
EXNAM Primary Examiner: Ford, John M.
LREP Johnston, George W., Epstein, William H., Parise, John P.
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1715
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **179400-23-8P 179400-32-9P**
(prepn. of N-(phenoxypyrimidinyl)heteroarom. sulfonamides as endothelin antagonists)
RN 179400-23-8 USPATFULL

CN 2-Thiophenesulfonamide, 5-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]-(9CI) (CA INDEX NAME)



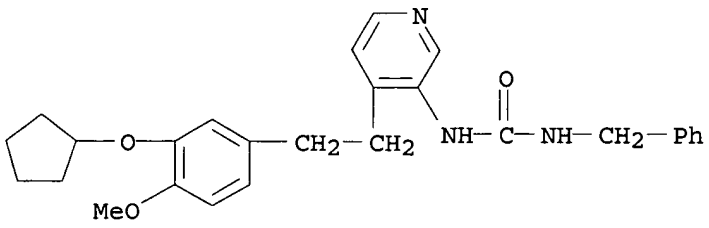
RN 179400-32-9 USPATFULL
CN 2-Pyridinesulfonamide, N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]-5-(1-methylethyl)- (9CI) (CA INDEX NAME)



L3 ANSWER 7 OF 8 USPATFULL
AB Compounds of general formula (1) ##STR1## are described wherein Y is a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; X is --O--, --S-- or --N(R.sup.7)--, where R.sup.7 is a hydrogen atom or an alkyl group; R.sup.2 is an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 and R.sup.4, which may be the same or different, is each a hydrogen atom or an alkyl, --CO.sub.2 R.sup.8 (where R.sup.8 is a hydrogen atom or an alkyl, aryl, or aralkyl group), --CONR.sup.9 R.sup.10 (where R.sup.9 and R.sup.10 which may be the same or different is each a hydrogen atom or an alkyl, aryl or aralkyl group), --CSNR.sup.9 R.sup.10, --CN, --CH.sub.2 CN group; Z is --(CH.sub.2).sub.n -- (where n is zero or an integer 1, 2 or 3; R.sup.5 is an optionally substituted monocyclic or bicyclic aryl

group optionally containing one or more heteroatoms selected from oxygen, sulphur or nitrogen atoms; R.sup.6 is a hydrogen atom or a hydroxyl group; and the salts, solvates, hydrates, prodrugs and N-oxides thereof. Compounds according to the invention are potent and selective phosphodiesterase type IV inhibitors and are useful in the prophylaxis and treatment of diseases such as asthma where an unwanted inflammatory response or muscular spasm is present.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:39535 USPATFULL
TI Trisubstituted phenyl derivatives
IN Warrellow, Graham John, Northwood, United Kingdom
Cole, Valerie Anne, Burnham, United Kingdom
Alexander, Rikki Peter, High Wycombe, United Kingdom
PA Celltech Therapeutics Limited, Slough, United Kingdom (non-U.S. corporation)
PI US 5739144 19980414
AI US 1995-543962 19951017 (8)
RLI Continuation of Ser. No. US 1995-384612, filed on 2 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-208656, filed on 9 Mar 1994, now abandoned
PRAI GB 1993-4920 19930310
DT Utility
FS Granted
EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: Keys, Rosalynd
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1604
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **159196-19-7P**
(prepn. of heterocyclic trisubstituted Ph derivs. as phosphodiesterase inhibitors)
RN 159196-19-7 USPATFULL
CN Urea, N-[4-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethyl]-3-pyridinyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)

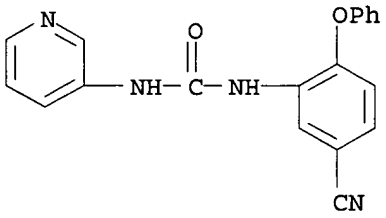



L3 ANSWER 8 OF 8 USPATFULL
AB Compounds having the formula ##STR1## and pharmaceutically acceptable salts thereof wherein X is a single bond, O, CO, S, NH or N(lower alkyl); Y is O, S or NCN; and R.sup.1 to R.sup.5' are as defined herein. These compounds have potassium channel activating activity and are useful, therefore for example, as cardiovascular agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 96:75411 USPATFULL

Print selected from Online session09/09/2002

TI Aryl urea and related compounds
IN Atwal, Karnail S., Newtown, PA, United States
Ferrara, Francis N., Martinsville, NJ, United States
Ding, Charles Z., Plainsboro, NJ, United States
PA Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)
PI US 5547966 19960820
AI US 1993-134195 19931007 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.
LREP Park, Ellen K.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 911
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **166263-16-7P**
(prepn. of biaryl ureas and analogs as cardiovascular agents)
RN 166263-16-7 USPATFULL
CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)

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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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=> s l2
L4          26 L2

=>
=> s l4  not L3
            26 L2
L5           0 L4 NOT L3

=> d his

     (FILE 'HOME' ENTERED AT 16:36:35 ON 09 SEP 2002)

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L1               STRUCTURE UPLOADED
L2            71 S L1 FUL

     FILE 'USPATFULL, USPAT2' ENTERED AT 16:37:15 ON 09 SEP 2002
L3             8 S L2

     FILE 'CAPLUS' ENTERED AT 16:37:54 ON 09 SEP 2002
L4            26 S L2
L5             0 S L4  NOT L3

=> s l4 not l3
            26 L2
L6           0 L4 NOT L3

=> d abs bib fhitstr l4 1-26

L4   ANSWER 1 OF 26  CAPLUS  COPYRIGHT 2002 ACS
GI
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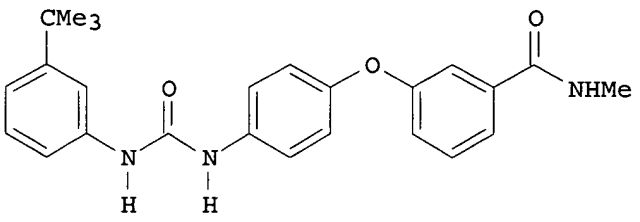



II

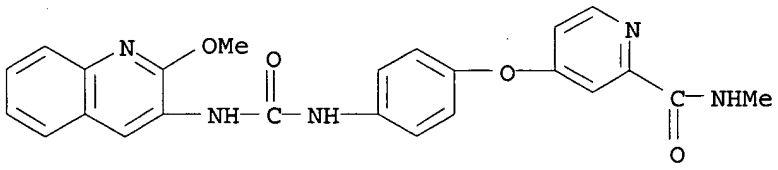
AB Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepd. Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (prepn. given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compd. II. Data for biol. activity of title compds. were given.

AN 2002:615574 CAPLUS
TI Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors
IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.
PA Bayer Corporation, USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2002062763 | A2 | 20020815 | WO 2002-US203361 | 20020207 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-777920 A 20010207
IT **432050-22-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)
RN 432050-22-1 CAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[(2-methoxy-3-quinolinyl)amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

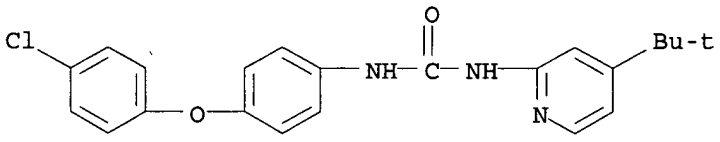



L4 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB This invention relates to the use of a group of heteroaryl ureas (I; for example, N-(2-methoxy-3-quinolyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea) contg. N in treating p38 mediated diseases, and pharmaceutical compns. for use in such therapy. I is A-NHC(O)NH-B or a pharmaceutically acceptable salt thereof, wherein A is a substituted or unsubstituted pyridyl, quinolinyl or isoquinolinyl group, B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 50 C atoms with a cyclic structure bound directly to N, contg. at least 5 cyclic members with 0-4 members of groups consisting of N, O and S. Information about the substituents for A and B are given in the claims. Although the methods of prepn. are not claimed, 37 example prepns. are included as well as examples of prepn. of intermediates. No pharmacol. data is included.

AN 2002:409267 CAPLUS
DN 137:6098
TI Heteroaryl ureas containing nitrogen hetero-atoms as p38 kinase inhibitors
IN Dumas, Jacques; Riedl, Bernd; Khire, Uday; Sibley, Robert N.; Hatoum-Mokdad, Holia; Monahan, Mary-katherine; Gunn, David E.; Lowinger, Timotthy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.
PA Bayer Corporation, USA
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U. S. Ser. No. 778,039.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

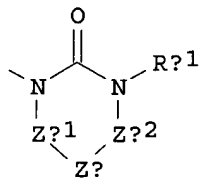
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2002065296 | A1 | 20020530 | US 2001-838286 | 20010420 |
| PRAI | US 1999-115878P | P | 19990113 | | |
| | US 1999-257265 | B1 | 19990225 | | |
| | US 1999-425229 | A2 | 19991022 | | |
| | US 2001-778039 | A2 | 20010207 | | |

OS MARPAT 137:6098
IT **432050-20-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl ureas contg. nitrogen hetero-atoms as p38 kinase inhibitors)
RN 432050-20-9 CAPLUS
CN Urea, N-[4-(4-chlorophenoxy)phenyl]-N'-[4-(1,1-dimethylethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)




L4 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

Q=



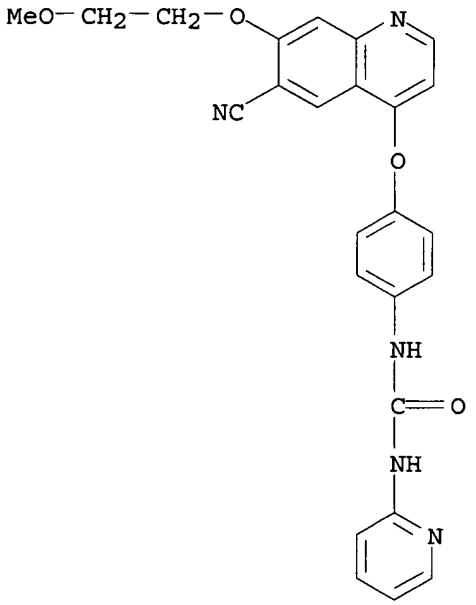

AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to

14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2)faCH:CH(CH2)fb (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliph. hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having .gtoreq.1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepd. These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to soln. of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temp. for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

AN 2002:314913 CAPLUS
DN 136:340689
TI Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis
IN Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki, Yasuyuki; Arimoto, Itaru
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 699 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002032872 | A1 | 20020425 | WO 2001-JP9221 | 20011019 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | JP 2000-320420 | A | 20001020 | | |
| | JP 2000-386195 | A | 20001220 | | |
| | JP 2001-46685 | A | 20010222 | | |

OS MARPAT 136:340689
IT **417712-95-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea derivs. contg. nitrogenous arom. ring compds. as angiogenesis inhibitors for prevention or treatment of diseases)
RN 417712-95-9 CAPLUS
CN Urea, N-[4-[[6-cyano-7-(2-methoxyethoxy)-4-quinolinyl]oxy]phenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2002 ACS
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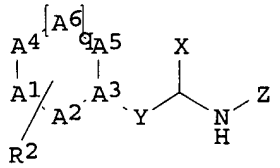

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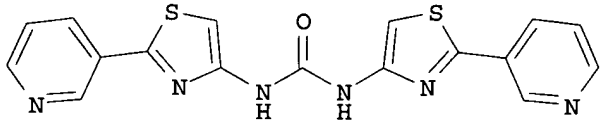


II

AB The title compds. [I; A1-A6 = CH2, CH, C, O, S, Nh, N; X and Z taken together to form a N atom contg. ring; Y = NHCO(CH2)p, CH2CO2, NHSO2CH2, NHCO2, NHCONR6(CH2)r; R2 = alkylaminoalkynyl, cycloalkenylalkynyl, phenylalkynyl, etc.; p = 1-2; q = 0-1; r = 0-3; R6 is not defined] which are effective for prophylaxis and treatment of diseases, such as cell proliferation or apoptosis mediated diseases involving stroke, cancer and the like, were prepd. Thus, treating 3-(3-pyridyl)-4-thiazolylcarbonylazide in PhMe with a few drops of H2O afforded the urea II which showed cdk2/cyclin and cdk5/cyclin kinase activity with IC50 of < 50 .mu.M.

AN 2002:142704 CAPLUS

DN 136:200177

TI Preparation of diheteroaryl ureas as antitumor agents

IN Santora, Vent; Askew, Benny; Ghose, Arup; Hague, Andrew; Kim, Tae Seong; Laber, Ellen; Li, Aiwen; Lian, Brian; Liu, Gang; Norman, Mark Henry; Smith, Leon; Tasker, Andrew; Tegley, Christopher; Yang, Kevin

PA Amgen Inc., USA

SO PCT Int. Appl., 371 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

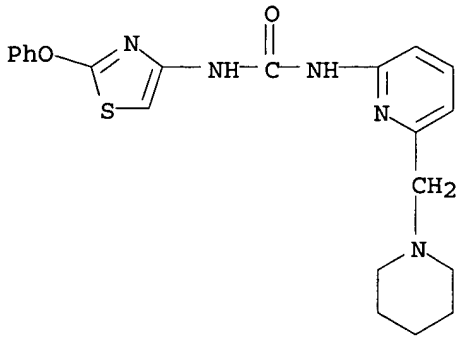
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002014311 | A2 | 20020221 | WO 2001-US25472 | 20010815 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2001084909 | A5 | 20020225 | AU 2001-84909 | 20010815 |
| PRAI | US 2000-225793P | P | 20000815 | | |
| | WO 2001-US25472 | W | 20010815 | | |

OS MARPAT 136:200177

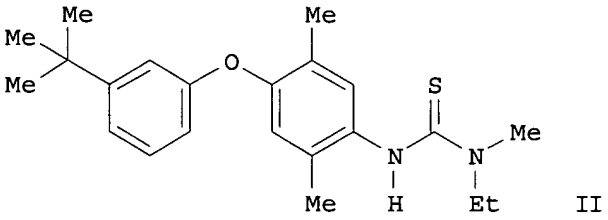
IT **400773-51-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diheteroaryl ureas as antitumor agents)

RN 400773-51-5 CAPLUS

CN Urea, N-(2-phenoxy-4-thiazolyl)-N'-[6-(1-piperidinylmethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



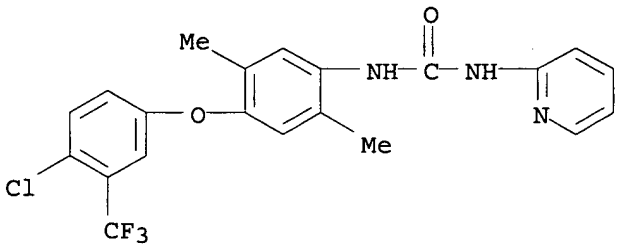
L4 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



AB R6ZZ1NRC(:X)R5 [I; R = H, alkyl, etc.; R5 = NR1R2, OR3, SR3; R1,R2 = H, alkyl, acyl, etc.; RR1, RR3, R1R2 = atoms to complete a ring; R3 = H, alkyl, etc.; R6 = 2-benzothienyl, 5-tert-butyl-1,3,4-oxadiazol-2-yl, substituted Ph, etc.; X = O or S; Z = bond, O, CO, SO0-2, NH, etc.; Z1 = e.g., 2,5-dimethyl-1,4-phenylene] were prepd. Thus, 2-chloro-1,4-xylene was nitrated and the product etherified by 3-(Me3C)C6H4OH to give, after redn., the phenoxyanilline which was treated with Cl2CS and the product amidated by HNMeEt to give title compd. II. Data for biol. activity of I were given.
AN 2002:104657 CAPLUS
DN 136:151003
TI Preparation of N-[(aryloxy)phenyl](thio)ureas and -carbamates as agrochemical fungicides
IN Gerusz, Vincent; Mansfield, Darren James; Perez, Jose; Tickle, David; Vors, Jean-Pierre; Baldwin, Derek; Hough, Thomas; Mitchell, Dale Robert
PA Aventis Cropscience S.A., Fr.
SO Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

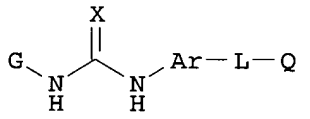
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 1178039 | A1 | 20020206 | EP 2001-420173 | 20010801 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| FR 2812633 | A1 | 20020208 | FR 2000-10305 | 20000804 |

JP 2002114751 A2 20020416 JP 2001-238513 20010806
PRAI FR 2000-10305 A 20000804
OS MARPAT 136:151003
IT **395658-94-3P**
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[(aryloxy)phenyl](thio)ureas and -carbamates as agrochem. fungicides)
RN 395658-94-3 CAPLUS
CN Urea, N-[4-[4-chloro-3-(trifluoromethyl)phenoxy]-2,5-dimethylphenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)




RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

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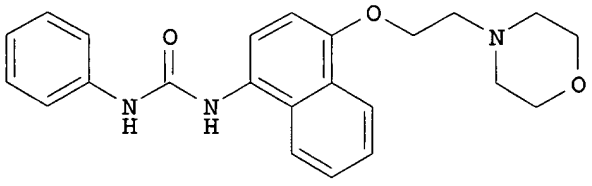



II

AB Title compds. (I) [wherein G = (un)substituted (non)arom. carbocycle or heterocycle; Ar = (un)substituted Ph, (tetrahydro)naphthyl, (tetrahydro)quinolinyl, (tetrahydro)isoquinolinyl, (dihydro)benzofuranyl, dihydrobenzothienyl, indolenyl, benzothiophenyl, benzimidazolyl, indanyl, indenyl, or indolyl; L = (un)substituted (un)satd. C chain with one or more methylene groups optionally independently replaced by O, N, or S(O)m; Q = (un)substituted Ph, naphthyl, pyridinyl, pyrimidinyl, pyridazinyl, (benz)imidazolyl, furanyl, thenyl, pyranyl, etc.; m = 0-2; X = O or S] were prepd. as cytokine prodn. inhibitors for use as non-steroidal anti-inflammatory agents. Thus, 4-[2-(morpholin-4-yl)ethoxy]naphth-1-

ylamine was treated sequentially with phosgene and 5-tert-butyl-2-methylaniline in CH2Cl2 to give II (42%). In a cytokine prodn. inhibition assay, II inhibited TNF.alpha. in lipopolysaccharide stimulated THP cells with IC50 < 10 .mu.M.

AN 2001:380570 CAPLUS

DN 135:5453

TI Preparation of aromatic heterocyclic substituted urea derivatives as non-steroidal anti-inflammatory agents

IN Breitfelder, Steffen; Cirillo, Pier F.; Hao, Ming-Hong; Hickey, Eugene R.; Sharma, Rajiv; Sun, Sanxing; Takahashi, Hidenori

PA Boehringer Ingelheim Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

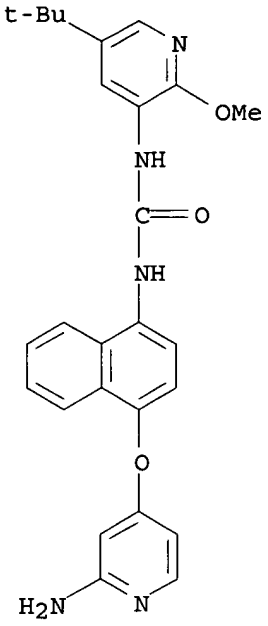
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001036403 | A1 | 20010525 | WO 2000-US31582 | 20001116 |
| | W: AE, AU, BG, BR, BY, CA, CN, CZ, EE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| | EP 1232150 | A1 | 20020821 | EP 2000-978751 | 20001116 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR | | | | |
| PRAI | US 1999-165903P | P | 19991116 | | |
| | WO 2000-US31582 | W | 20001116 | | |

OS MARPAT 135:5453

IT **340825-57-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. heterocyclic substituted urea derivs. as cytokine inhibitors for use as non-steroidal anti-inflammatory agents)

RN 340825-57-2 CAPLUS

CN Urea, N-[4-[(2-amino-4-pyridinyl)oxy]-1-naphthalenyl]-N'-[5-(1,1-dimethylethyl)-2-methoxy-3-pyridinyl]- (9CI) (CA INDEX NAME)




RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Z = O, S; R1 = alkyl, alkenyl, alkoxy, etc.; R2-R6 = alkyl, alkenyl, alkoxy, etc.; adjacent pair of R2-R6 together with the carbon atoms to which they are attached form (un)substituted carbocyclyl, heterocyclyl; R7 = alkyl, alkenyl, alkoxy, etc.; n = 0-3] and their pharmaceutically acceptable salts which are non-peptide antagonists of human orexin receptors, in particular orexin-1 receptors, were prepd. E.g., treatment of 4-amino-2-methylquinoline with carbonyl diimidazole in CH2Cl2 followed by addn. of 6-amino-2-methylbenzoxazole afforded II which showed pKb > 6.0 against orexin-1 receptor. In particular, compds. I are of potential use in the treatment of obesity including obesity obsd. in Type 2(non-insulin-dependent) diabetes patients and/or sleep disorders.
AN 2000:573791 CAPLUS
DN 133:164009
TI Preparation of phenyl ureas and thioureas as orexin receptor antagonists
IN Coulton, Steven; Johns, Amanda; Porter, Roderick Alan
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000047577 | A1 | 20000817 | WO 2000-EP1150 | 20000210 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1150977 A1 20011107 EP 2000-906324 20000210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI GB 1999-3266 A 19990212
GB 1999-26430 A 19991108
WO 2000-EP1150 W 20000210

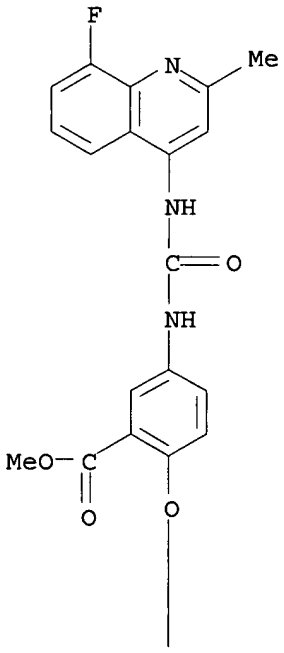
OS MARPAT 133:164009

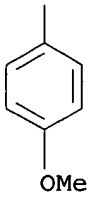
IT **288151-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of Ph ureas and thioureas as orexin receptor antagonists)

RN 288151-08-6 CAPLUS

CN Benzoic acid, 5-[[[(8-fluoro-2-methyl-4-quinolinyl)amino]carbonyl]amino]-2-(4-methoxyphenoxy)-, methyl ester (9CI) (CA INDEX NAME)

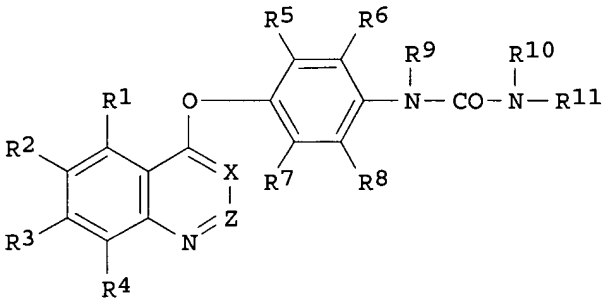
PAGE 1-A






RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI




I

AB Title compds. [I; X and Z represent each CH or N; R1-3 represent each H, optionally substituted alkoxy, etc.; R4 represents H; R5-8 represent each H, halogeno, alkyl, alkoxy, alkylthio, nitro or amino, provided that all of R5-8 do not represent H simultaneously; R9 and R10 represent each H, alkyl or alkylcarbonyl; and R11 represents alkyl, alkenyl, alkynyl or aralkyl], pharmaceutically acceptable salts and solvates, and medicinal compns. contg. the same are prepd. and tested having antitumor activity and causing no morphol. change in cells. Thus, the title compd. I (X = CH; Z = CH; R1, R4, R5,R7-R10 each an H; R11 = 3,5-F2C6H3) was prepd. and tested.

AN 2000:513673 CAPLUS

DN 133:135235

TI Preparation and anti-tumor, anti-atherosclerosis, anti-psoriasis, anti-diabetes, and anti-arthritis activities of quinolines and quinazolines

IN Kubo, Kazuo; Fujiwara, Yasunari; Isoe, Toshiyuki

PA Kirin Beer Kabushiki Kaisha, Japan

SO PCT Int. Appl., 208 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000043366 | A1 | 20000727 | WO 2000-JP255 | 20000120 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| | BR 2000007656 | A | 20011030 | BR 2000-7656 | 20000120 |
| | EP 1153920 | A1 | 20011114 | EP 2000-900841 | 20000120 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | NO 2001002617 | A | 20010914 | NO 2001-2617 | 20010529 |
| PRAI | JP 1999-14858 | A | 19990122 | | |
| | JP 1999-26691 | A | 19990203 | | |
| | JP 1999-142493 | A | 19990521 | | |
| | JP 1999-253624 | A | 19990907 | | |
| | WO 2000-JP255 | W | 20000120 | | |

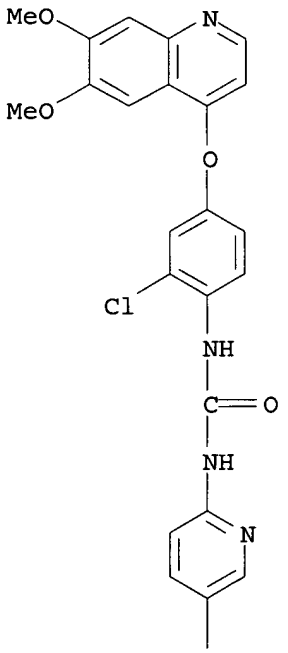
OS MARPAT 133:135235

IT **286369-67-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antitumor activity of quinolines and quinazolines)

RN 286369-67-3 CAPLUS

CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)

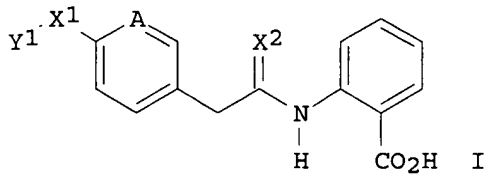
PAGE 1-A



Cl

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



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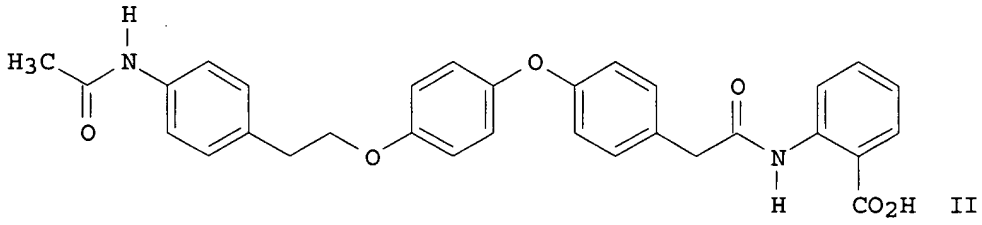


II

AB Title compds. [I; wherein Y1 = a group represented by (un)substituted-Ph, (un)substituted-2-naphthyl; X1 is O, S; X2 is O or S; A = CH, N] and stereoisomers are prepd. and tested as antagonists of IgE antibody, therefore useful as preventive or therapeutic agents for allergic diseases and having cytotoxic activities useful as antitumor agents. The title compd. II was prepd.

AN 2000:84754 CAPLUS
DN 132:151571
TI Preparation of anthranilic acid derivatives as preventive or therapeutic agents
IN Tsuchiya, Naoki; Takeuchi, Susumu; Takeyasu, Takumi; Hase, Naoki; Yamori, Takao; Tsuruo, Takashi
PA Teijin Limited, Japan
SO PCT Int. Appl., 213 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000005198 | A1 | 20000203 | WO 1999-JP3969 | 19990723 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| AU 9948004 | A1 | 20000214 | AU 1999-48004 | 19990723 |
| EP 1101755 | A1 | 20010523 | EP 1999-931522 | 19990723 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI JP 1998-209410 | A | 19980724 | | |
| JP 1998-258486 | A | 19980911 | | |
| JP 1998-369808 | A | 19981225 | | |
| JP 1998-369809 | A | 19981225 | | |
| WO 1999-JP3969 | W | 19990723 | | |

OS MARPAT 132:151571

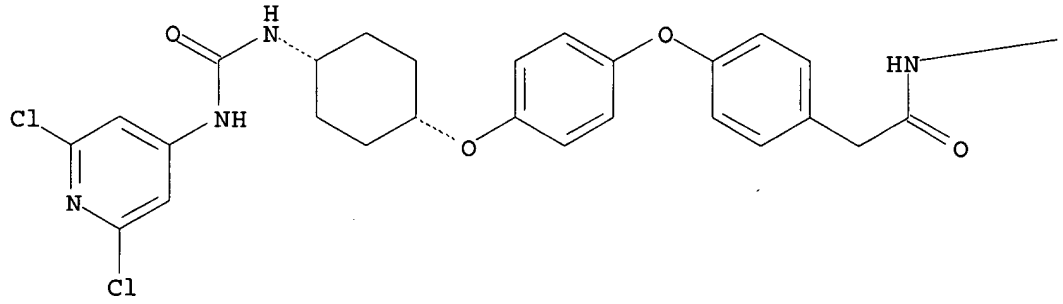
IT **257606-70-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of anthranilic acid derivs. as preventive or therapeutic agents)

RN 257606-70-5 CAPLUS

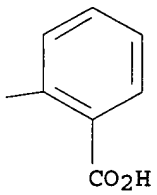
CN Benzoic acid, 2-[[[4-[4-[[cis-4-[[[(2,6-dichloro-4-pyridinyl)amino]carbonyl]amino]cyclohexyl]oxy]phenoxy]phenyl]acetyl]amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A




PAGE 1-B




RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2002 ACS
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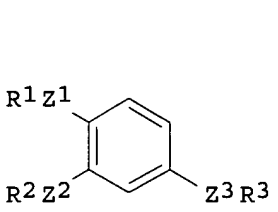
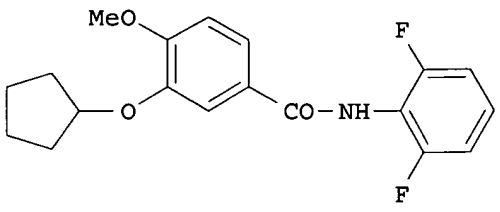



I




II

AB Title compds. (I) [R1 = lower alkyl; R2 = (un)substituted cycloalkyl, (un)substituted cycloalkenyl, (un)substituted or oxidized cyclothioalkyl, or (un)substituted or oxidized cyclothioalkenyl; R3 = (un)substituted (hetero)aryl; Z, Z1, Z2 = independently O or S; Z3 = C(:Z)NH] and their N-oxides and salts were prepd. for pharmaceutical use as tumor necrosis factor and cAMP phosphodiesterase inhibitors. Thus, 3-cyclopentyloxy-4-methoxybenzoyl chloride (prepn. given) in CH2Cl2 was added dropwise to 2,6-difluoroaniline in triethylamine and CH2Cl2 and refluxed for 4 h to yield N-(2,6-difluorophenyl)-3-cyclopentyloxy-4-methoxybenzamide (II). Compds. of the invention were tested for inhibitory effects on PDE activity and eosinophil superoxide generation, effects on tracheal smooth muscle contractility, in vivo bronchodilator actions and antigen(ovalbamin)-induced eosinophilia, in vitro inhibitory effects on TNF-.alpha. release by human monocytes, and inhibitory effects on antigen-induced bronchoconstriction in conscious guinea-pigs and serum TNF-.alpha. levels in LPS-challenged mice. Compds. showed 10,000-fold to 50-fold more selectivity for cAMP phosphodiesterase IV than cyclic nucleotide phosphodiesterase types I, III, or V and have IC50 values ranging from 0.1 nM to 40 .mu.M for PDE activity. At concns. from 5x10-9M to 10-5M, preferably 5x10-9 to 10-7, compds. produced about 50% relaxation of guinea-pig tracheal strips. When administered at EDs of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. produced 30% to 90% decrease in bronchospasm without any significant effect on blood pressure. At oral doses of 1 to 50 mg/kg, preferably 1 to 10 mg/kg, and inhaled doses of 4 to 1000 .mu.g/kg, preferably 4 to 50 .mu.g/kg, compds. inhibited by at least 50% ovalbumin-induced eosinophilia in guinea-pigs. Compds. produced 50% inhibition of LPS-induced TNF-.alpha. release from human PBMs at concns. of 10-9M to 10-6M, preferably 10-9M to 10-8 M. At doses of 1 to 1000 .mu.g/kg (i.t.), preferably 1 to 20 .mu.g/kg (i.t.), compds. inhibited antigen-induced bronchoconstriction by up to 80%. Compds. inhibited LPS-induced serum TNF-.alpha. at doses of 10 to 10,000 .mu.g/kg, preferably 10 to 250 .mu.g/kg. Compds. showed very low mammalian toxicity levels. Twenty-one compns. of the title compds. for gelatin capsules or dry powder inhalers were also prepd.

AN 1999:505666 CAPLUS
DN 131:144417

TI N-(Hetero)aryl-3,4-(cyclo)alkoxybenzamides and analogs useful as tumor necrosis factor and c-AMP phosphodiesterase inhibitors

IN Fenton, Garry; Morley, Andrew David; Palfreyman, Malcolm Norman; Ratcliffe, Andrew James; Harp, Brian William; Thurairatnam, Sukanthini; Vacher, Bernard Yvon Jack; Ashton, Michael John; Cook, David Charles; Hills, Susan Jacqueline; McFarlane, Ian Michael; Vicker, Nigel
PA Rhone-Poulenc Rorer Ltd., UK

SO U.S., 48 pp.
CODEN: USXXAM
DT Patent
LA English

FAN.CNT 3

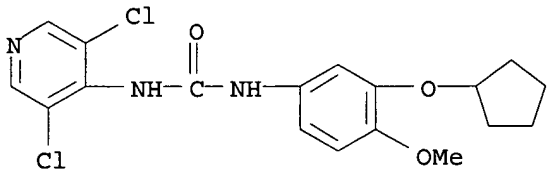
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5935978 | A | 19990810 | US 1993-98178 | 19930728 |
| | ZA 9200547 | A | 19930503 | ZA 1992-547 | 19920127 |
| | WO 9212961 | A1 | 19920806 | WO 1992-GB153 | 19920128 |
| | W: AU, CA, CS, FI, HU, JP, KR, NO, PL, RU, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | AU 9211881 | A1 | 19920827 | AU 1992-11881 | 19920128 |
| | AU 664694 | B2 | 19951130 | | |
| | EP 569414 | A1 | 19931118 | EP 1992-903462 | 19920128 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | JP 06504782 | T2 | 19940602 | JP 1992-503280 | 19920128 |
| | PL 169994 | B1 | 19960930 | PL 1992-300142 | 19920128 |
| | CZ 281894 | B6 | 19970312 | CZ 1993-1528 | 19920128 |
| | NO 9302701 | A | 19930921 | NO 1993-2701 | 19930727 |
| | ZA 9305448 | A | 19940519 | ZA 1993-5448 | 19930728 |
| | FI 9500375 | A | 19950127 | FI 1995-375 | 19950127 |
| | US 5679696 | A | 19971021 | US 1995-484805 | 19950607 |
| | US 5698711 | A | 19971216 | US 1995-487377 | 19950607 |
| | US 5840724 | A | 19981124 | US 1997-881888 | 19970624 |
| | US 6255326 | B1 | 20010703 | US 1999-239075 | 19990127 |
| | US 6096768 | A | 20000801 | US 1999-301877 | 19990429 |
| PRAI | GB 1991-1777 | A | 19910128 | | |
| | GB 1991-17727 | A | 19910816 | | |
| | WO 1992-GB153 | B2 | 19920128 | | |
| | GB 1992-15989 | A | 19920728 | | |
| | GB 1992-16005 | A | 19920728 | | |
| | GB 1992-16006 | A | 19920728 | | |
| | GB 1992-16008 | A | 19920728 | | |
| | GB 1992-16764 | A | 19920807 | | |
| | GB 1993-10633 | A | 19930521 | | |
| | GB 1993-10938 | A | 19930527 | | |
| | GB 1993-11281 | A | 19930601 | | |
| | GB 1993-14847 | A | 19930716 | | |
| | US 1993-98178 | A3 | 19930728 | | |
| | US 1995-484805 | A3 | 19950607 | | |

OS MARPAT 131:144417

IT **159782-49-7P**, N-(3,5-Dichloropyrid-4-yl)-N'-(3-cyclopentyloxy-4-methoxyphenyl)urea
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl 3,4-(cyclo)alkoxybenzamides and analogs useful as tumor necrosis factor and c-AMP phosphodiesterase inhibitors)

RN 159782-49-7 CAPLUS

CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)




RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2002 ACS
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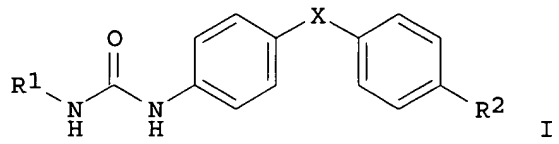

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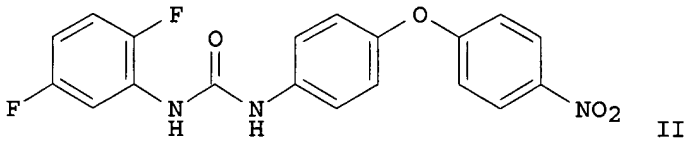

II

AB The invention relates to 1,3-disubstituted ureas I [R1 = (un)substituted aryl; R2 = NO2, NH2; X = O, S], and a method of prepg. them by treating arom. amines with isocyanates. The isocyanates may be formed in situ, and the reaction carried out in a solvent such as toluene, at, e.g., 80.degree.C. If a nitro group is formed, it may be reduced with H2 in the presence of a Pd catalyst to give an amino group. The obtained 1,3-disubstituted ureas are inhibitors of the activity of the enzyme acyl co-enzyme A:cholesterol acyltransferase (ACAT), and may be used to inhibit cholesterol esterification and absorption in hypercholesterolemia. For instance, reaction of 4-(4'-nitrophenoxy)aniline with 2,5-difluorophenyl isocyanate gave 76% title compd. II. The latter gave 49% inhibition of rat liver ACAT at 2 .mu.M, and 58% inhibition of ACAT in rabbit intestinal mucosa, at the same concn., both in vitro.

AN 1999:421643 CAPLUS
DN 131:73441
TI 1,3-Disubstituted ureas useful as ACAT inhibitors, and method for their preparation
IN Oremus, Vladimir; Smahovsky, Vendelin; Faberova, Viera; Kakalik, Ivan; Schmidtova, Ludmila; Zemanek, Marian
PA Slovako- Farma, A.S., Slovakia
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9932437 | A1 | 19990701 | WO 1998-SK19 | 19981216 |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| | AU 9916976 | A1 | 19990712 | AU 1999-16976 | 19981216 |
| | EP 1042278 | A1 | 20001011 | EP 1998-961715 | 19981216 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO | | | | |
| | JP 2001526259 | T2 | 20011218 | JP 2000-525374 | 19981216 |
| | US 6444691 | B1 | 20020903 | US 2000-581821 | 20000710 |
| PRAI | SK 1997-1751 | A | 19971219 | | |
| | WO 1998-SK19 | W | 19981216 | | |

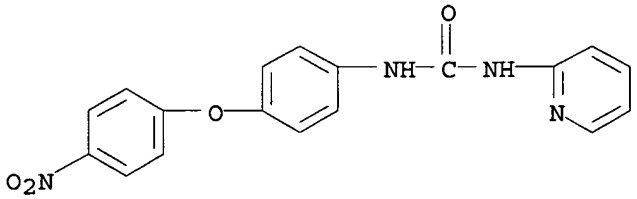
OS MARPAT 131:73441

IT **228544-41-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1,3-disubstituted ureas as ACAT inhibitors)

RN 228544-41-0 CAPLUS

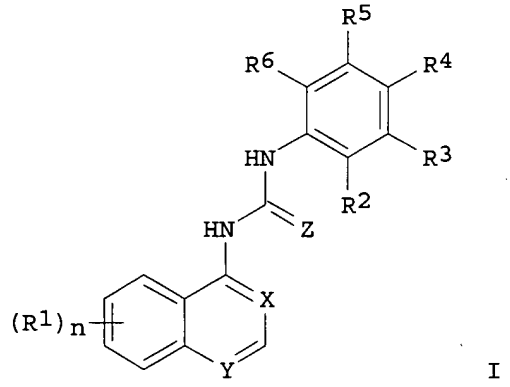
CN Urea, N-[4-(4-nitrophenoxy)phenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2002 ACS

GI



I

AB Title compds. [I; X, Y = CH, N, provided that X and Y do not both = CH; Z = O, S; R1 = halo, R7CO, R8R9NCO, (substituted) alkyl, alkenyl, alkoxy; R2-R6 = H, halo, NO2, cyano, aryloxy, arylalkyloxy, arylalkyl, R7CO, R7SO2NH, R7CONR10, NR8R9, NR8R9CO, COR8, heterocyclyl, (substituted) alkyl, alkenyl, alkoxy, alkylthio, provided that .gtoreq.1 of R2-R6 is other than H; an adjacent pair of R2- R6 = atoms to form a (substituted)

carbocyclic or heterocyclic ring; R7 = alkyl, aryl; R8, R9 = H, alkyl, aryl, aralkyl; R10 = H, alkyl; n = 0-4], were prepd. Thus, quinoline-4-carbonyl azide (prepn. given) was refluxed 1 h in PhMe; 5-amino-1-methylindole in CH2Cl2 was added and the mixt. was stirred 16 h at room temp. to give 1-(1-methyl-1H-indol-5-yl)-3-quinolin-4-ylurea. The latter showed pKb >7 in an assay of human HFGAN72 antagonist activity.

AN 1999:139841 CAPLUS

DN 130:196581

TI Preparation of quinolinylureas and related compounds as HFGAN72 antagonists.

IN Chan, George; Johns, Amanda; Jurewicz, Anthony; Porter, Roderick Alan; Widdowson, Katherine

PA Smithkline Beecham Plc, UK

SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

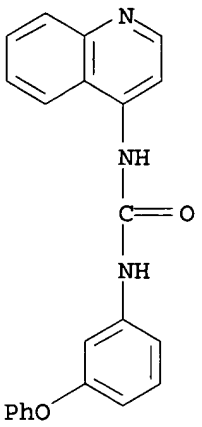
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9909024 | A1 | 19990225 | WO 1998-GB2437 | 19980813 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2300178 | AA | 19990225 | CA 1998-2300178 | 19980813 |
| | AU 9887411 | A1 | 19990308 | AU 1998-87411 | 19980813 |
| | EP 1003737 | A1 | 20000531 | EP 1998-938812 | 19980813 |
| | R: BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| | JP 2001515075 | T2 | 20010918 | JP 2000-509705 | 19980813 |
| | US 6410529 | B1 | 20020625 | US 2000-485623 | 20000510 |
| PRAI | GB 1997-17178 | A | 19970814 | | |
| | GB 1998-7756 | A | 19980408 | | |
| | WO 1998-GB2437 | W | 19980813 | | |

OS MARPAT 130:196581

IT **220844-29-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinolinylureas and related compds. as HFGAN72 antagonists)

RN 220844-29-1 CAPLUS

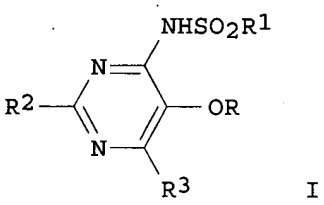
CN Urea, N-(3-phenoxyphenyl)-N'-4-quinolinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB Title compds. [I; R = (un)substituted Ph; R1 = heterocyclyl (sic); R2 = H, alkyl, alkoxy, Ph, etc.; R3 = CHO, (un)substituted alkyl, alkoxy, etc.] were prepd. Thus, 4,6-dichloro-5-(2-methoxyphenoxy)-2,2'-bipyrimidine was condensed with 5-tert-butylthiophene-2-sulfonamide K salt and the product etherified by (HOCH2)2 to give I [R = OC6H4(OMe)-2, R1 = 5-tert-butyl-2-thienyl, R2 = 2-pyrimidinyl, R3 = OCH2CH2OH]. Data for biol. activity of I were given.
AN 1998:749411 CAPLUS
DN 130:13993
TI Preparation of N-(phenoxypyrimidinyl)heteroaromatic sulfonamides as endothelin antagonists
IN Breu, Volker; Burri, Kaspar; Cassal, Jean-marie; Clozel, Martine; Hirth, Georges; Loffler, Bernd-michael; Muller, Marcel; Neidhart, Werner; Ramuz, Henri
PA Hoffmann-La Roche Inc., USA
SO U.S., 17 pp., Cont.-in-part of U. S. Ser. No. 676,313.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| PI | US 5837708 | A | 19981117 | US 1996-730422 | 19961015 |
| | WO 9616963 | A1 | 19960606 | WO 1995-CH131 | 19950606 |
| | W: CH, US | | | | |
| | ZA 9509808 | A | 19960527 | ZA 1995-9808 | 19951117 |
| | BR 9505528 | A | 19971104 | BR 1995-5528 | 19951127 |
| PRAI | CH 1994-3559 | A | 19941125 | | |
| | WO 1995-CH131 | A | 19950606 | | |
| | US 1996-676313 | A2 | 19960718 | | |

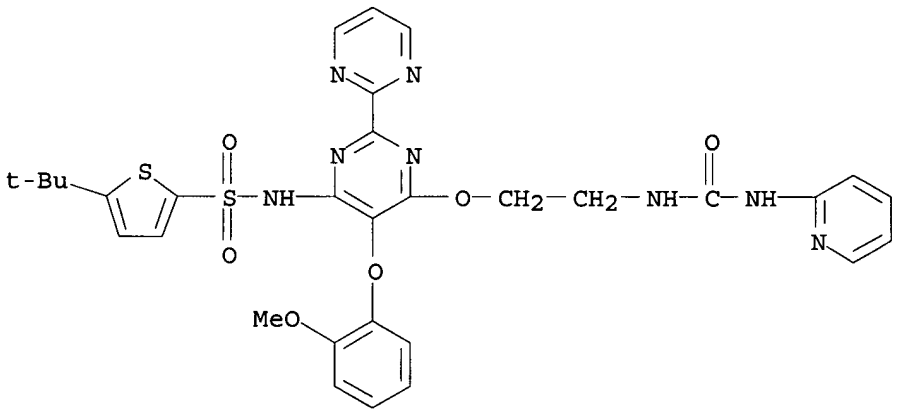
OS MARPAT 130:13993

IT **179400-23-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(phenoxypyrimidinyl)heteroarom. sulfonamides as endothelin antagonists)

RN 179400-23-8 CAPLUS

CN 2-Thiophenesulfonamide, 5-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]- (9CI) (CA INDEX NAME)




RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2002 ACS

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

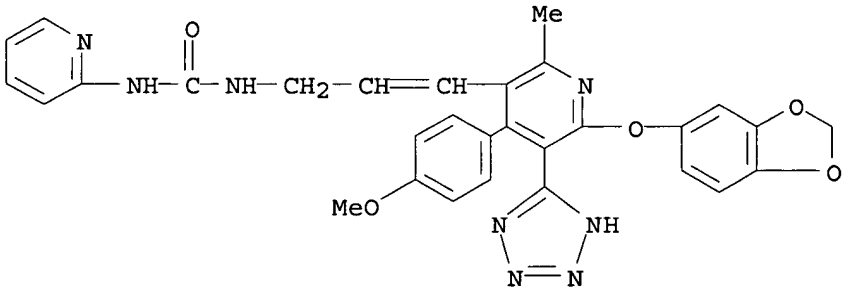
AB The title compds. (I; R1 - R11 = H, halo, OH, NH2, NO2, lower alkyl, alkoxy, alkenyl, alkylamino, alkylthio, alkanoyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkenyl, haloalkyl, haloalkoxy, or haloalkenyl, aryl-lower alkoxy, aroyl; or two of R1 - R5 groups or two of R7 - R11 groups are linked to each other to form a ring; R6 = an acidic functional group; R12 = aryl, heteroaryl, heterocyclylcarbonyl, or groups listed for R1 - R5 and R7 - R11; X = CR13R14, NR15, O, S; Y = NR16, O, S, CR17:CR18; R13 - R18 = H, lower alkyl; Z = H, OH, CO2H, lower alkoxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylcarbamoyl, arylcarbamoyl,

heteroarylcarbamoyl, NH2, alkylamino, arylamino, heteroarylamino, acylamino, O2CNR19R20, NR21CONR22R23, O-CO2R24, NR25CO2R26, OR27, O2CR28; R19 - R28 = H, lower alkyl, aryl, heteroaryl; or R19 and R20, R21 and R22, R21 and R23, R22 and R23, or R25 and R26 are bonded to each other to form a ring; m = 0,1; n = 0-3) are prepd. They are useful for the treatment of hypertension, Raynaud's disease, acute kidney failure, myocardial infarction, angina pectoris, cerebral infarction, atrophy of brain blood vessels, arteriosclerosis, bronchial asthma, stomach ulcer, acute liver failure, diabetes, endotoxin shock, multi-organ failure, disseminated intravascular agglutination, and/or cyclosporin-induced kidney disorders. Thus, 3-cyano-5-(3-hydroxy-1-propenyl)-4-(4-methoxyphenyl)-6-methyl-2-(3,4-methylenedioxyphenyl)pyridine was dissolved in toluene, treated with Bu3SnN3, and refluxed overnight to give 60.5% the title 4-phenyl-3-tetrazolylpyridine compd. (II). II in vitro inhibited the binding of [125I]endotoxin to a pig ventricular muscle membrane prepn. with a -pIC50 value of 8.1.

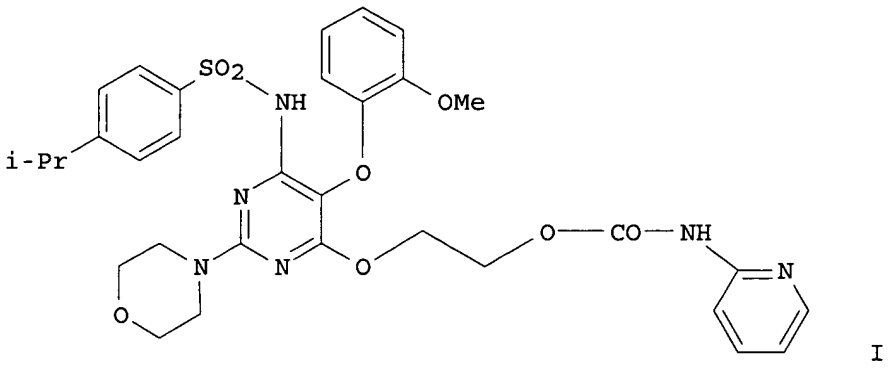
AN 1998:81044 CAPLUS
DN 128:192655
TI Preparation of 4-phenylpyridine derivatives as endothelin antagonists
IN Sakurai, Kuniya; Niwa, Seiji; Oono, Seiji; Uchita, Hirohisa
PA Ajinomoto Co., Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 95 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 10029979 | A2 | 19980203 | JP 1997-93782 | 19970411 |
| PRAI JP 1996-91272 | | 19960412 | | |

OS MARPAT 128:192655
IT **203802-04-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylpyridine derivs. as endothelin antagonists for treatment endothelin-related diseases)
RN 203802-04-4 CAPLUS
CN Urea, N-[3-[6-(1,3-benzodioxol-5-yloxy)-4-(4-methoxyphenyl)-2-methyl-5-(1H-tetrazol-5-yl)-3-pyridinyl]-2-propenyl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)




L4 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



I

AB Implementation of a pyridylcarbamoyl group and an isopropylpyridylsulfonamide substituent as key components in the scaffold of Bosentan resulted in the identification of the potent orally active endothelin receptor antagonist Ro 48-5695 (I). It shows affinities for ETA and ETB receptors in the low nanomolar range and high functional antagonistic potency in vitro.

AN 1997:633849 CAPLUS

DN 127:307357

TI Discovery of RO 48-5695: a potent mixed endothelin receptor antagonist optimized from bosentan

AU Neidhart, Werner; Breu, Volker; Burri, Kaspar; Clozel, Martine; Hirth, Georges; Klinkhammer, Uwe; Giller, Thomas; Ramuz, Henri

CS Pharma Div., Preclinical Res., F. Hoffmann-La Roche Ltd., Basel, CH-4070, Switz.

SO Bioorganic & Medicinal Chemistry Letters (1997), 7(17), 2223-2228
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

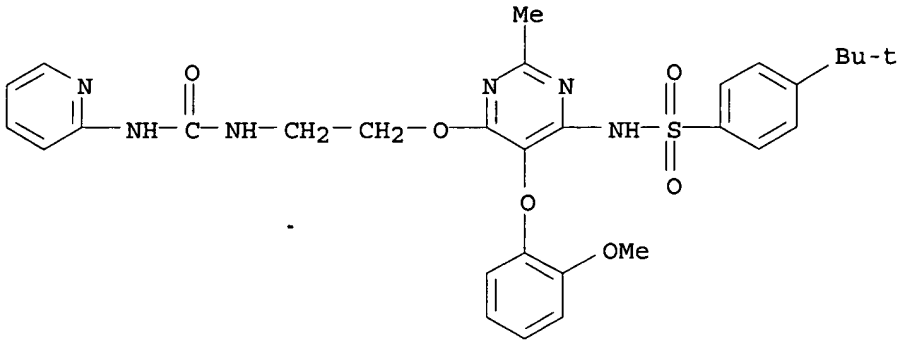
DT Journal

LA English

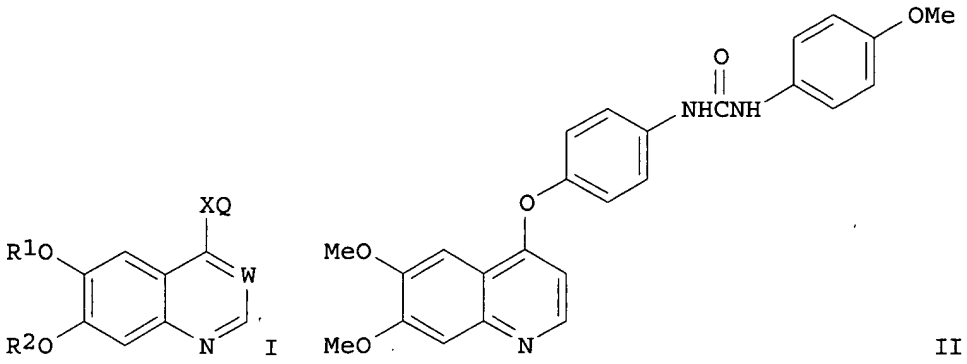
IT **167403-34-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of RO 48-5695, a potent mixed endothelin receptor antagonist optimized from bosentan)

RN 167403-34-1 CAPLUS

CN Benzenesulfonamide, 4-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-2-methyl-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI



AB The title compds. I [R1 and R2 represent each H or C1-4 alkyl, or R1 and R2 together form C1 to C3 alkylene; X represents O, S or CH2; W represents CH or N; and Q represents substituted aryl or substituted heteroaryl] are prepd. I inhibit platelet-derived growth factor receptor autophosphorylation and are useful in the treatment of cancer, arthritis, etc. The title compd. II (prepn. given) (at 100 mg/kg i.p. once daily for 9 days) increased the survival of mice with transplanted leukemic P388 cells by 130%.

AN 1997:414195 CAPLUS

DN 127:34137

TI Preparation of quinoline and quinazoline derivatives inhibiting platelet-derived growth factor receptor autophosphorylation

IN Kubo, Kazuo; Ohyama, Shinichi; Shimizu, Toshiyuki; Nishitoba, Tsuyoshi; Kato, Shinichiro; Murooka, Hideko; Kobayashi, Yoshiko; et al.

PA Kirin Beer Kabushiki Kaisha, Japan; Kubo, Kazuo; Ohyama, Shinichi; Shimizu, Toshiyuki; Nishitoba, Tsuyoshi; Kato, Shinichiro

SO PCT Int. Appl., 243 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

| | | | | | |
|---|---|---|---|---|---|
| PI | WO 9717329 | A1 | 19970515 | WO 1996-JP3229 | 19961105 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9673400 | A1 | 19970529 | AU 1996-73400 | 19961105 |
| | EP 860433 | A1 | 19980826 | EP 1996-935541 | 19961105 |
| | EP 860433 | B1 | 20020703 | | |
| | R: CH, DE, FR, GB, LI | | | | |
| | US 6143764 | A | 20001107 | US 1998-68660 | 19980506 |
| PRAI | JP 1995-313555 | A | 19951107 | | |
| | JP 1996-62121 | A | 19960223 | | |
| | WO 1996-JP3229 | W | 19961105 | | |

OS MARPAT 127:34137

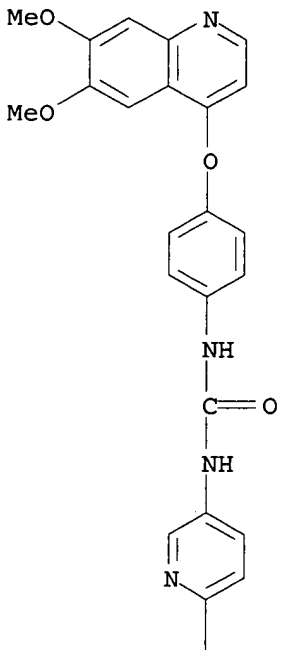
IT **190727-92-5P**

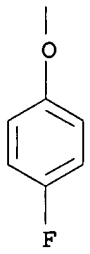
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline and quinazoline derivs. inhibiting platelet-derived growth factor receptor autophosphorylation)

RN 190727-92-5 CAPLUS

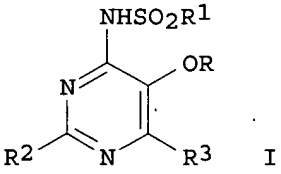
CN Urea, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[6-(4-fluorophenoxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A






L4 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI




I

AB Title compds. [I; R = (un)substituted Ph; R1 = heterocyclyl; R2 = H, alkyl, alkoxy, Ph, heterocyclyl, etc.; R3 = alkyl, alkoxy, CHO, etc.] were prepd. Thus, 5-tert-butyl-2-thiophenesulfonamide was N-arylated by 4,6-dichloro-5-(2-methoxyphenoxy)-2,2'-bipyrimidine and the product etherified by HOCH2CH2OH to give I [R = 1g(OMe)-2, R1 = 5-tert-butyl-2-thienyl, R2 = 2-pyrimidinyl, R3 = OCH2CH2OH]. Data for inhibition of endothelin-induced rat aorta contraction by 2 prepd. I were given.

AN 1996:469485 CAPLUS

DN 125:114678

TI Preparation of N-(4-pyrimidinyl)sulfonamides as endothelin receptor antagonists

IN Breu, Volker; Burri, Kaspar; Cassal, Jean-Marie; Clozel, Martine; Hirth, Georges; Loeffler, Bernd-Michael; Mueller, Marcel; Neidhart, Werner; Ramuz, Henri

PA F. Hoffmann-La Roche Ag, Switz.

SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 713875 | A1 | 19960529 | EP 1995-117833 | 19951113 |
| | EP 713875 | B1 | 20010321 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | CA 2162630 | AA | 19960526 | CA 1995-2162630 | 19951110 |
| | AT 199905 | E | 20010415 | AT 1995-117833 | 19951113 |
| | ES 2156179 | T3 | 20010616 | ES 1995-117833 | 19951113 |
| | AU 9537895 | A1 | 19960530 | AU 1995-37895 | 19951116 |
| | AU 691353 | B2 | 19980514 | | |
| | ZA 9509808 | A | 19960527 | ZA 1995-9808 | 19951117 |

| | | | | | |
|---|---|---|---|---|---|
| | JP 08208625 | A2 | 19960813 | JP 1995-300933 | 19951120 |
| | JP 2755565 | B2 | 19980520 | | |
| | HU 75030 | A2 | 19970328 | HU 1995-3311 | 19951120 |
| | IL 116064 | A1 | 20000629 | IL 1995-116064 | 19951120 |
| | NO 9504718 | A | 19960528 | NO 1995-4718 | 19951122 |
| | CZ 289920 | B6 | 20020417 | CZ 1995-3088 | 19951123 |
| | FI 9505669 | A | 19960526 | FI 1995-5669 | 19951124 |
| | CN 1132751 | A | 19961009 | CN 1995-120250 | 19951124 |
| | CN 1064965 | B | 20010425 | | |
| | TW 394763 | B | 20000621 | TW 1995-84112546 | 19951124 |
| | RU 2162084 | C2 | 20010120 | RU 1995-120013 | 19951124 |
| | BR 9505528 | A | 19971104 | BR 1995-5528 | 19951127 |
| PRAI | CH 1994-3559 | A | 19941125 | | |
| | CH 1995-2842 | A | 19951009 | | |

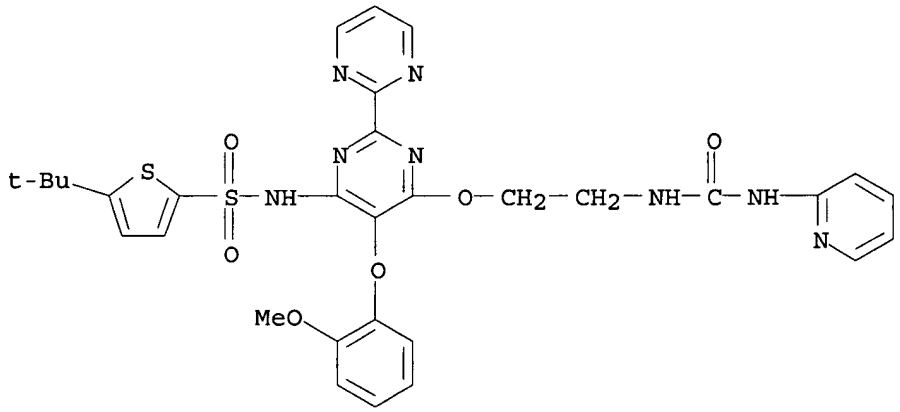
OS MARPAT 125:114678

IT **179400-23-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(4-pyrimidinyl)sulfonamides as endothelin receptor antagonists)

RN 179400-23-8 CAPLUS

CN 2-Thiophenesulfonamide, 5-(1,1-dimethylethyl)-N-[5-(2-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy][2,2'-bipyrimidin]-4-yl]- (9CI) (CA INDEX NAME)




L4 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2002 ACS

AB R4YC6H4(CH2)nNR2CONHR3 [R2 = (ar)alkyl, heterocyclyl(alkyl), alkoxyalkyl, etc.; R3,R4 = (un)substituted aryl, heterocyclyl; Y = bond, alkylene, O, CO, CONH, etc.; n = 0 or 1] were prep. Thus, 1-cycloheptyl-1-(4-phenoxyphenylmethyl)-3-(2,4,6-trifluorophenyl)urea had IC50 of 1.1x10-8M against cholesterol acyltransferase in vitro.

AN 1996:455768 CAPLUS

DN 125:114322

TI Preparation of urea derivatives as cholesterol acyltransferase inhibitors

IN Terasawa, Takeshi; Tanaka, Akira; Chiba, Toshiyuki; Takasugi, Hisashi

PA Fujisawa Pharmaceutical Co., Ltd., Japan

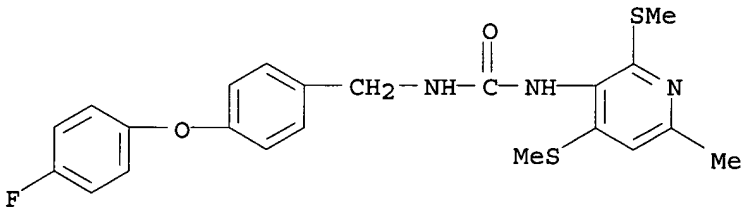
SO PCT Int. Appl., 228 pp.
CODEN: PIXXD2

DT Patent

LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9610559 | A1 | 19960411 | WO 1995-JP1982 | 19950929 |
| | W: AU, CA, CN, HU, JP, KR, MX, RU, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | CA 2200981 | AA | 19960411 | CA 1995-2200981 | 19950929 |
| | AU 9535779 | A1 | 19960426 | AU 1995-35779 | 19950929 |
| | EP 784612 | A1 | 19970723 | EP 1995-932934 | 19950929 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| | JP 10510512 | T2 | 19981013 | JP 1995-511616 | 19950929 |
| | ZA 9508365 | A | 19960508 | ZA 1995-8365 | 19951004 |
| PRAI | GB 1994-19970 | | 19941004 | | |
| | GB 1995-6720 | | 19950331 | | |
| | GB 1995-14021 | | 19950710 | | |
| | WO 1995-JP1982 | | 19950929 | | |

OS MARPAT 125:114322
IT **179057-08-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of urea derivs. as cholesterol acyltransferase inhibitors)
RN 179057-08-0 CAPLUS
CN Urea, N-[[4-(4-fluorophenoxy)phenyl]methyl]-N'-[6-methyl-2,4-bis(methylthio)-3-pyridinyl]- (9CI) (CA INDEX NAME)




L4 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2002 ACS
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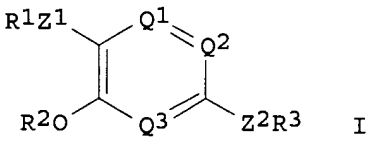


I

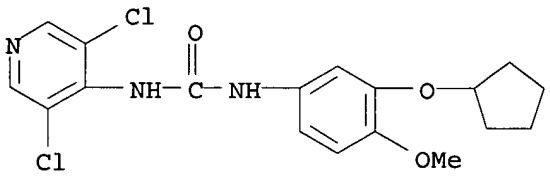
AB The title compds. [I; Q1-Q3 = N, CX, CH; X = halogen; R1 = (un)substituted lower alkyl group; R2 = (un)substituted oxaaliph.; R3 = (un)substituted aryl or heteroaryl; Z1 = O, S; Z2 = CH:CH, C.tplbond.C, CH2CZ, CZCH2, CZCZ, CH2NH, CH2O, CH2S, CX2O, CZNH, NHCH2, OCH2, SCH2, SOCH2, SO2CH2, OCX2, OCZ, NHCZ, N:N, NHSO2, SO2NH, SO2NH, CZCZNH, NHCOO, OCONH, NHCONH; Z = O, S] [e.g., N-(3,5-dichloro-1-oxido-4-pyridino)-4-difluoromethoxy-3-(tetrahydro-3-furyloxy)benzamide, m.p. 169-171.degree. (decompn.)], useful for inhibiting the prodn. or physiol. effects of tumor necrosis factor and inhibiting cyclic-AMP phosphodiesterase, are prepd. and I-contg.

formulations presented. I demonstrate phosphodiesterase IC50 values of 0.1 nM to 40 .mu.M.

AN 1995:994180 CAPLUS
DN 124:55798
TI Preparation of substituted (hetero)aromatic compounds as cyclic-AMP phosphodiesterase and TNF inhibitors
IN Fenton, Garry; Palfreyman, Malcolm Norman; Thurairatnam, Sukanthini
PA Rhone-Poulenc Rorer Ltd., UK
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9520578 | A1 | 19950803 | WO 1995-GB157 | 19950126 |
| | W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US | | | | |
| | RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9514631 | A1 | 19950815 | AU 1995-14631 | 19950126 |
| | ZA 9500639 | A | 19960726 | ZA 1995-639 | 19950126 |
| | EP 741707 | A1 | 19961113 | EP 1995-906437 | 19950126 |
| | EP 741707 | B1 | 19980401 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | JP 09509654 | T2 | 19970930 | JP 1995-519939 | 19950126 |
| | AT 164575 | E | 19980415 | AT 1995-906437 | 19950126 |
| PRAI | GB 1994-1460 | | 19940126 | | |
| | WO 1995-GB157 | | 19950126 | | |

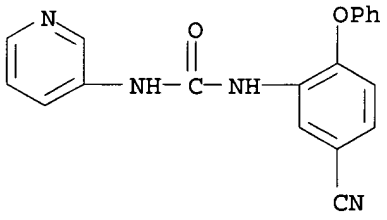
OS MARPAT 124:55798
IT **159782-49-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted (hetero)arom. compds. as cyclic-AMP phosphodiesterase and TNF inhibitors)
RN 159782-49-7 CAPLUS
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)




L4 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB The results of the efforts aimed at the replacement of the benzopyran ring of the lead cardiac selective antiischemic ATP-sensitive potassium channel (KATP) opener (I) are described. Systematic modification of the benzopyran ring of I resulted in the discovery of a structurally simpler acyclic analog (II) with slightly lower antiischemic potency than I.

Further structure-activity studies on the acyclic analog II provided the 2-phenoxy-3-pyridylurea analog (III) with improved antiischemic potency and selectivity compared to the benzopyran-based I. These data demonstrate that the benzopyran ring of I and its congeners is not mandatory for antiischemic activity and cardiac selectivity. The results described also show that, as for the benzopyran class of compds., the structure-activity relations for the antiischemic and vasorelaxant activities of KATP openers are distinct. The mechanism of action of the acyclic analogs (e.g., III) still appears to involve KATP opening as their cardioprotective effects are abolished by pretreatment with the KATP blocker glyburide.

AN 1995:983072 CAPLUS
DN 124:75535
TI Cardioselective Antiischemic ATP-Sensitive Potassium Channel Openers. 4. Structure-Activity Studies on Benzopyranylcyanoguanidines: Replacement of the Benzopyran Portion
AU Atwal, Karnail S.; Ferrara, Francis N.; Ding, Charles Z.; Grover, Gary J.; Sleph, Paul G.; Dzwonczyk, Steven; Baird, Anne J.; Normandin, Diane E.
CS Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, NEW JERSEY, USA
SO Journal of Medicinal Chemistry (1996), 39(1), 304-13
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **166263-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-activity studies of potassium channel opener benzopyranylcyanoguanidines)
RN 166263-16-7 CAPLUS
CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)




L4 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2002 ACS
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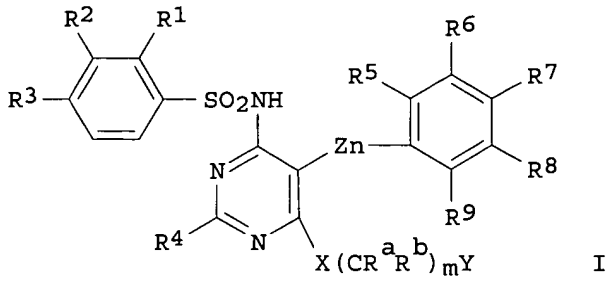


I

AB Title compds. (I; R1-R3 = H, alkyl, alkoxy, alkylthio, alkenyl, halo, CF3, hydroxyalkoxy, haloalkoxy, alkanoylalkyl, hydroxyalkyl, CO2H, amino, etc.; R2R3, R5R6, R6R7 = butadienyl, methylenedioxy, ethylenedioxy, isopropylidenedioxy; R4 = H, alkyl, cycloalkyl, CF3, alkoxy, alkynyloxy, alkylthio, alkylthioalkyl, hydroxyalkyl, dihydroxyalkoxy, alkylsulfinyl, alkylsulfonyl, aryl, arylthio, aryloxy, heterocyclyl, heterocyclylalkyl, etc.; R5-R9 = H, halo, CF3, alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl; Ra, Rb = H, alkyl, alkoxy, alkylthio; X = O, S, NH; Y = O2CNR10R11, HNOCNR10R11, O2COR10, HNCO2R10; R10 = alkyl, cycloalkyl, hydroxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, alkanoyloxyalkyl, arylcarbamoylalkyl, heterocyclyl, heterocyclylalkyl, etc.; R11 = H, R10; m = 1-3; n = 0,1), were prepd. Thus, 2-pyridinecarbonyl azide was heated in PhMe; 4-tert-butyl-N-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2,2'-bipyrimidin-4-yl]benzenesulfonamide was added to give pyridine-2-carbaminic acid, 2-[6-(4-tert-butylphenylsulfonylamino)-5-(2-methoxyphenoxy)-2,2'-bipyrimidin-4-yloxy]ethyl ester. The latter at 30 mg/kg orally in rats gave a 30% redn. in av. arterial blood pressure.

AN 1995:780258 CAPLUS

DN 123:169647

TI Preparation of sulfonylaminopyrimidines as endothelin antagonists.

IN Breu, Volker; Burri, Kaspar; Cassal, Hean-Marie; Clozel, Martine; Hirth, Georges; Loeffler, Bernd-Michael; Mueller, Marcel; Neidhart, Werner; Ramuz, Henri

PA F. Hoffmann-La Roche AG, Switz.

SO Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 633259 | A1 | 19950111 | EP 1994-109257 | 19940616 |
| | EP 633259 | B1 | 19990113 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | TW 394761 | B | 20000621 | TW 1994-83105221 | 19940608 |
| | CA 2125730 | AA | 19941229 | CA 1994-2125730 | 19940613 |
| | AT 175669 | E | 19990115 | AT 1994-109257 | 19940616 |
| | ES 2127850 | T3 | 19990501 | ES 1994-109257 | 19940616 |
| | ZA 9404434 | A | 19950103 | ZA 1994-4434 | 19940621 |
| | IL 110089 | A1 | 20000831 | IL 1994-110089 | 19940622 |
| | AU 9465948 | A1 | 19950105 | AU 1994-65948 | 19940624 |
| | AU 678467 | B2 | 19970529 | | |
| | HU 67636 | A2 | 19950428 | HU 1994-1907 | 19940624 |
| | FI 9403084 | A | 19941229 | FI 1994-3084 | 19940627 |
| | NO 9402428 | A | 19941229 | NO 1994-2428 | 19940627 |
| | BR 9402558 | A | 19950328 | BR 1994-2558 | 19940627 |

| | | | | | |
|---|---|---|---|---|---|
| | CN 1106007 | A | 19950802 | CN 1994-106574 | 19940627 |
| | CN 1050839 | B | 20000329 | | |
| | LT 3723 | B | 19960226 | LT 1994-1979 | 19940627 |
| | LV 11175 | B | 19960620 | LV 1994-131 | 19940627 |
| | US 5541186 | A | 19960730 | US 1994-266072 | 19940627 |
| | PL 175771 | B1 | 19990226 | PL 1994-304007 | 19940627 |
| | PL 177031 | B1 | 19990930 | PL 1994-323036 | 19940627 |
| | RU 2142457 | C1 | 19991210 | RU 1994-22258 | 19940627 |
| | CZ 287184 | B6 | 20001011 | CZ 1994-1573 | 19940627 |
| | JP 07017972 | A2 | 19950120 | JP 1994-146003 | 19940628 |
| | JP 2545200 | B2 | 19961016 | | |
| | RO 114325 | B3 | 19990330 | RO 1994-1112 | 19940628 |
| | SK 280736 | B6 | 20000711 | SK 1994-779 | 19940628 |
| PRAI | CH 1993-1924 | A | 19930628 | | |
| | IL 1992-101650 | A0 | 19920420 | | |
| | CH 1994-1575 | A | 19940520 | | |

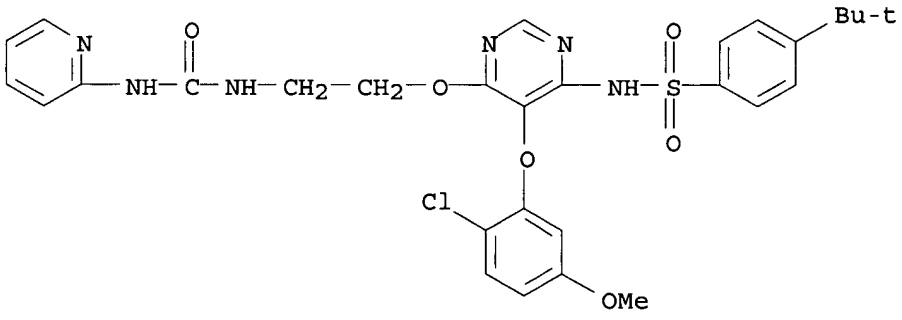
OS MARPAT 123:169647

IT **167403-30-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonylaminopyrimidines as endothelin antagonists)

RN 167403-30-7 CAPLUS

CN Benzenesulfonamide, N-[5-(2-chloro-5-methoxyphenoxy)-6-[2-[[(2-pyridinylamino)carbonyl]amino]ethoxy]-4-pyrimidinyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)




L4 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2002 ACS

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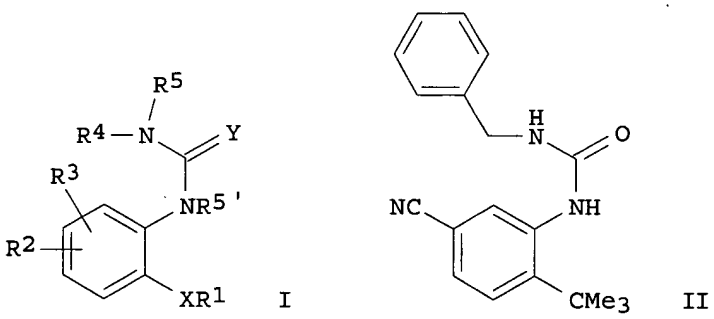

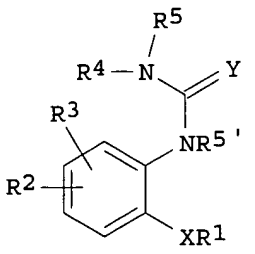

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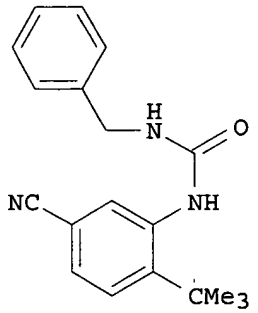


II

AB Title compds. I [X = single bond, O, CO, S, NH, or alkylimino; Y = O, S, or NCN; R1 = alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; R2 = H, alkyl, haloalkyl, alkenyl, alkynyl, cyano, NO2, CHO, CO2H, halo, (un)substituted amino, etc.; R3 = H, alkyl, OH, alkoxy, (un)substituted amino, cyano, NO2; R4 = aryl, aralkyl, heterocyclo, heterocycloalkyl; R5, R5' = H, alkyl, (un)substituted alkylamino, haloalkyl; or R4R5 form ring with 5 to 7 members and optional O, S, or (un)substituted NH] and salts are claimed, along with 18 specific compds. which were also prepd. These compds. have potassium channel activating activity and are useful, e.g., as cardiovascular agents (no data). For example, tert-butylbenzene underwent 2,4-dinitration (70%), redn. of the 4-nitro group to amino (86%), diazotization and cyanation of the group to give a benzonitrile (42%), and redn. of the remaining nitro group with SnCl2 (100%) to give 3-amino-4-(tert-butyl)benzonitrile. Reaction of this with benzyl isocyanate gave title compd. II in 70% yield.

AN 1995:733459 CAPLUS

DN 123:143653

TI Biaryl ureas and related compounds for use as cardiovascular agents.

IN Atwal, Karnail; Ferrara, Francis N.; Ding, Charles Z.

PA USA

SO Can. Pat. Appl., 39 pp.
CODEN: CPXXEB

DT Patent

LA English

FAN.CNT 1

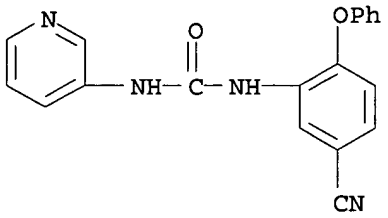
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | CA 2132771 | AA | 19950408 | CA 1994-2132771 | 19940923 |
| | US 5547966 | A | 19960820 | US 1993-134195 | 19931007 |
| | EP 656350 | A1 | 19950607 | EP 1994-306813 | 19940916 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | AU 9474463 | A1 | 19950427 | AU 1994-74463 | 19941006 |
| | AU 690133 | B2 | 19980423 | | |
| | JP 07188151 | A2 | 19950725 | JP 1994-243895 | 19941007 |
| PRAI | US 1993-134195 | | 19931007 | | |

OS MARPAT 123:143653

IT **166263-16-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biaryl ureas and analogs as cardiovascular agents)

RN 166263-16-7 CAPLUS

CN Urea, N-(5-cyano-2-phenoxyphenyl)-N'-3-pyridinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2002 ACS
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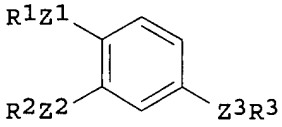

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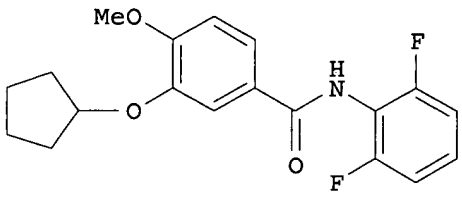

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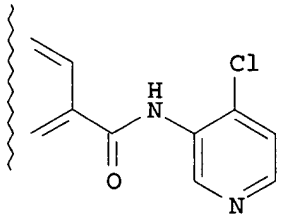


III

AB Title compds. I [R1 = alkyl; R2 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, cyclothioalkyl, cyclothioalkenyl; R3 = aryl, heteroaryl; Z, Z1, Z2 = O, S; Z3 = CH:CH, C.tplbond.C, CH2C(:Z), C(:Z)CH2, C(:Z)C(:Z), C(:Z)NH, NHC(:Z), CH2NH, CH2O, CH2S, CX2O, N:N, NHSO2, NHCO2, etc.; X = halo] and their N-oxides and salts, for manuf. of medicaments for treatment of a wide variety of disease states modulated by tumor necrosis factor (TNF) inhibitors, are claimed. The invention also includes pharmaceutical use of I for inhibiting cAMP phosphodiesterases (PDE). For example, amidation of either 2,6-difluoroaniline or 4-chloropyrid-3-ylamine with 3-cyclopentyloxy-4-methoxybenzoyl chloride gave title compds. II and III, resp. I had IC50 of 10-9 to 10-5M for inhibition of porcine PDE IV, and were 50- to 10,000-fold more selective for cAMP PDE type IV than for types I, III, or V. I also inhibited eosinophil superoxide generation, showed bronchodilator activity in several tests, and inhibited LPS-induced serum TNF-.alpha. in mice. Examples include 77 prepns. of I, 111 ref. prepns. of precursors, and 21 pharmaceutical formulations.

AN 1995:257708 CAPLUS

DN 122:290715

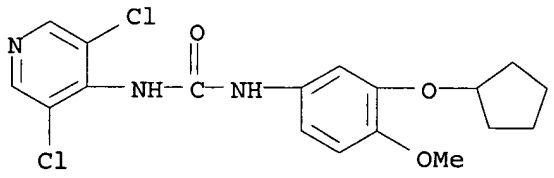
TI N-Phenyl- and N-pyridylbenzamides and analogs useful as inhibitors of c-AMP phosphodiesterase and TNF

IN Fenton, Garry; Morley, Andrew David; Palfreyman, Malcolm Norman; Ratcliffe, Andrew James; Sharp, Brian William; Stuttle, Keith Alfred

James; Thurairatnam, Sukanthini; Vacher, Bernard Yvon Jack
PA Rhone-Poulenc Rorer Ltd., UK
SO PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9402465 | A1 | 19940203 | WO 1993-GB1597 | 19930728 |
| | W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | ZA 9305448 | A | 19940519 | ZA 1993-5448 | 19930728 |
| | EP 652868 | A1 | 19950517 | EP 1993-917937 | 19930728 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | JP 08503925 | T2 | 19960430 | JP 1993-504330 | 19930728 |
| | HU 72656 | A2 | 19960528 | HU 1995-265 | 19930728 |
| | FI 9500375 | A | 19950127 | FI 1995-375 | 19950127 |
| | NO 9500319 | A | 19950327 | NO 1995-319 | 19950127 |
| PRAI | GB 1992-15989 | A | 19920728 | | |
| | GB 1992-16005 | A | 19920728 | | |
| | GB 1992-16006 | A | 19920728 | | |
| | GB 1992-16008 | A | 19920728 | | |
| | GB 1992-16764 | A | 19920807 | | |
| | GB 1993-10633 | A | 19930521 | | |
| | GB 1993-10938 | A | 19930527 | | |
| | GB 1993-11281 | A | 19930601 | | |
| | GB 1993-14847 | A | 19930716 | | |
| | WO 1993-GB1597 | W | 19930728 | | |

OS MARPAT 122:290715
IT **159782-49-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as inhibitor of c-AMP phosphodiesterase or TNF)
RN 159782-49-7 CAPLUS
CN Urea, N-[3-(cyclopentyloxy)-4-methoxyphenyl]-N'-(3,5-dichloro-4-pyridinyl)- (9CI) (CA INDEX NAME)




L4 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2002 ACS
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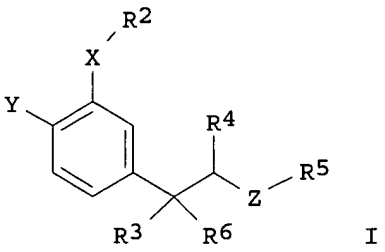


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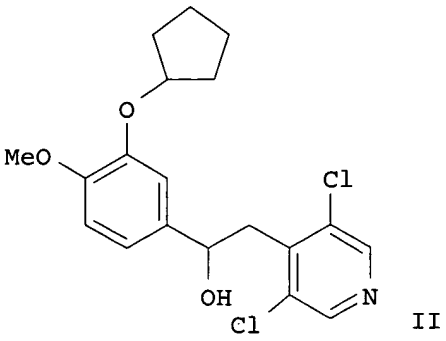



II

AB Title compds. I [wherein Y = halo or OR1; R1 = (un)substituted alkyl; X = O, S, or NR7, R7 = H, alkyl; R2 = (un)substituted cycloalkyl or cycloalkenyl; R3, R4 = H, alkyl, CO2R8 (where R8 = H, alkyl, aryl, or aralkyl), CONR9R10 (where R9, R10 = H, alkyl, aryl or aralkyl), CSNR9R10, cyano, CH2CN; Z = (CH2)n (where n = 0-3); R5 = (un)substituted mono- or bicyclic aryl group optionally contg. .gtoreq. 1 heteroatom(s) selected from O, S, or N; R6 = H or OH] and the salts, solvates, hydrates, prodrugs and N-oxides thereof are disclosed. The compds. are potent and selective inhibitors of phosphodiesterase (PDE) type IV, and are useful in the prophylaxis and treatment of diseases such as asthma, where unwanted inflammatory responses or muscular spasms are present. For example, lithiation of 3,5-dichloro-4-methylpyridine with LDA in THF at -70.degree., followed by reaction with 3-cyclopentyloxy-4-methoxybenzaldehyde, gave title compd. (.+-.)-II. I are said to show concn.-dependent inhibition of recombinant PDE IV at 0.1-1000 nM with little or no activity against PDE I, II, III, or V at up to 100 .mu.M. Prepns. of approx. 20 I and 20 intermediates, along with general ranges of results for addnl. biol. tests, are described.

AN 1995:207617 CAPLUS

DN 122:10065

TI Trisubstituted phenyl derivatives as phosphodiesterase inhibitors and processes for their preparation

IN Warrellow, Graham John; Cole, Valerie Anne; Alexander, Rikki Peter

PA Celltech Limited, UK

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9420446 | A1 | 19940915 | WO 1994-GB453 | 19940309 |
| | W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, UZ, VN | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2135480 | AA | 19940915 | CA 1994-2135480 | 19940309 |
| | AU 9461489 | A1 | 19940926 | AU 1994-61489 | 19940309 |
| | AU 675511 | B2 | 19970206 | | |
| | EP 640065 | A1 | 19950301 | EP 1994-908454 | 19940309 |
| | EP 640065 | B1 | 20011017 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | JP 08505158 | T2 | 19960604 | JP 1994-519748 | 19940309 |

| | | | | | |
|---|---|---|---|---|---|
| | AT 207051 | E | 20011115 | AT 1994-908454 | 19940309 |
| | ES 2162623 | T3 | 20020101 | ES 1994-908454 | 19940309 |
| | US 5739144 | A | 19980414 | US 1995-543962 | 19951017 |
| | US 5962483 | A | 19991005 | US 1998-8173 | 19980116 |
| PRAI | GB 1993-4920 | A | 19930310 | | |
| | US 1994-208656 | B1 | 19940309 | | |
| | WO 1994-GB453 | W | 19940309 | | |
| | US 1995-384612 | B1 | 19950202 | | |
| | US 1995-543962 | A3 | 19951017 | | |

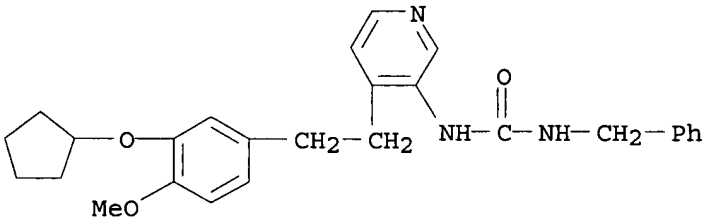
OS MARPAT 122:10065

IT **159196-19-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic trisubstituted Ph derivs. as phosphodiesterase inhibitors)

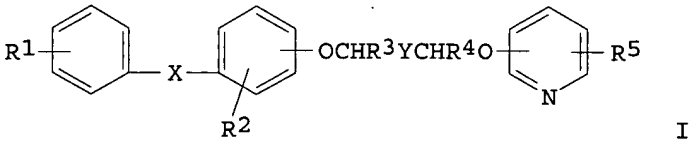
RN 159196-19-7 CAPLUS

CN Urea, N-[4-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethyl]-3-pyridinyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)




L4 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2002 ACS

GI




I

AB The title compds. I (R1 = H, halogen, alkyl, alkoxy, or haloalkyl; R2 = H, halogen, alkyl, alkenyl, haloalkyl, alkoxy, alkylthio, haloalkoxy, haloalkylthio; R3, R4 = H, alkyl, haloalkyl, alkoxyalkyl, alkenoxyalkyl, alkenyl, alkynyl, or together form a direct bond; R5 = H, halogen, alkyl, haloalkyl, alkoxy, NH2, alkyl, alkylamino, dialkylamino, or acylamino), as well as their salts, are prepd. for use as insecticides, esp. against fleas. Thus, Ph 4-[2-[2-(2-pyridyloxy)ethoxy)]ethoxy]phenyl ether (II) was prepd. by treating 2-[2-(4-phenoxyphenoxy)ethoxy]ethanol with 2-chloropyridine. II showed 100% activity against fleas both in vivo and in vitro tests.

AN 1990:458954 CAPLUS

DN 113:58954

TI Preparation of substituted pyridines as insecticides

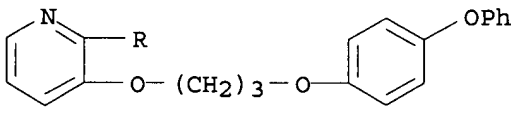
IN Alig, Bernd; Stendel, Wilhelm; Londershausen, Michael

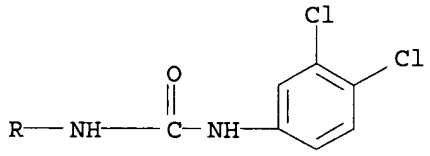
PA Bayer A.-G., Fed. Rep. Ger.

SO Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

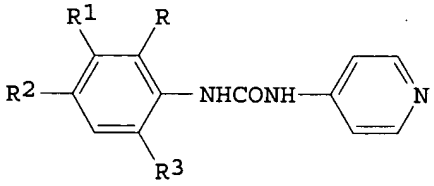
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 356797 | A2 | 19900307 | EP 1989-114980 | 19890812 |
| | EP 356797 | A3 | 19910403 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| | DE 3828820 | A1 | 19900322 | DE 1988-3828820 | 19880825 |
| | JP 02117660 | A2 | 19900502 | JP 1989-215127 | 19890823 |
| | DK 8904186 | A | 19900226 | DK 1989-4186 | 19890824 |
| | AU 8940252 | A1 | 19900405 | AU 1989-40252 | 19890824 |
| | AU 617513 | B2 | 19911128 | | |
| | BR 8904250 | A | 19900410 | BR 1989-4250 | 19890824 |
| | ZA 8906454 | A | 19900530 | ZA 1989-6454 | 19890824 |
| PRAI | DE 1988-3828820 | | 19880825 | | |

OS MARPAT 113:58954
IT **128262-28-2P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as insecticide)
RN 128262-28-2 CAPLUS
CN Urea, N-(3,4-dichlorophenyl)-N'-[3-[3-(4-phenoxyphenoxy)propoxy]-2-pyridinyl]- (9CI) (CA INDEX NAME)




L4 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2002 ACS
GI

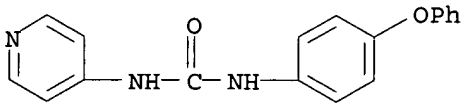



I

AB A series of N-phenyl-N'-pyridinylureas, e.g., I (R, R1, R2, R3 = H, Cl,

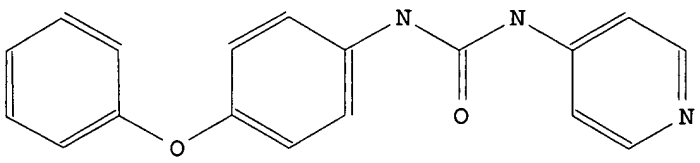
Br, F, CF3, Me, Et, CHMe2, NO2, NH2, OMe, etc.) was prepd. by the reaction of aryl isocyanates with 2-, 3-, of 4-aminopyridine. They were examd. for anticonvulsant activity. Extensive structure/activity investigations revealed optimal activity in the N-(2,6-disubstituted-phenyl)-N'-(4-pyridinyl)urea series, with I (R = Cl, R1 = R2 = H, R3 = Me) (II) exhibiting the best overall anticonvulsant profile. II was effective against seizures induced by maximal electroshock but did not protect mice from clonic seizures produced by the convulsant pentylenetetrazol. The overall pharmacol. profile suggests that II would be of therapeutic use in the treatment of generalized tonic-clonic and partial seizures. II was selected for Phase 1 clin. trials.

AN 1990:55554 CAPLUS
DN 112:55554
TI N-Phenyl-N'-pyridinylureas as anticonvulsant agents
AU Pavia, Michael R.; Lobbestael, Sandra J.; Taylor, Charles P.; Hershenson, Fred M.; Miskell, David L.
CS Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SO J. Med. Chem. (1990), 33(2), 845-61
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 112:55554
IT **124420-93-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and anticonvulsant activity of)
RN 124420-93-5 CAPLUS
CN Urea, N-(4-phenoxyphenyl)-N'-4-pyridinyl- (9CI) (CA INDEX NAME)



L8 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2002 BEILSTEIN CDS MDL

| | |
|---|---|
| Beilstein Records (BRN): | 3560216 |
| Beilstein Pref. RN (BPR): | 124420-93-5 |
| CAS Reg. No. (RN): | **124420-93-5** |
| Chemical Name (CN): | 1-(4-phenoxy-phenyl)-3-pyridin-4-yl-urea |
| Autonom Name (AUN): | 1-(4-phenoxy-phenyl)-3-pyridin-4-yl-urea |
| Molec. Formula (MF): | C18 H15 N3 O2 |
| Molecular Weight (MW): | 305.34 |
| Lawson Number (LN): | 27378, 14892, 5219, 1762 |
| Compound Type (CTYPE): | heterocyclic |
| Constitution ID (CONSID): | 3152373 |
| Tautomer ID (TAUTID): | 3387514 |
| Beilstein Citation (BSO): | 6-22 |
| Entry Date (DED): | 1991/10/23 |
| Update Date (DUPD): | 1993/03/20 |




Field Availability:

| Code | Name | Occurrence |
|---|---|---|
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| BPR | Beilstein Preferred RN | 1 |
| RN | CAS Registry Number | 1 |
| CN | Chemical Name | 1 |
| AUN | Autonomname | 1 |
| MF | Molecular Formula | 1 |
| FW | Formular Weight | 1 |
| LN | Lawson Number | 4 |
| CTYPE | Compound Type | 1 |
| CONSID | Constitution ID | 1 |
| TAUTID | Tautomer ID | 1 |
| BSO | Beilstein Citation | 1 |
| ED | Entry Date | 1 |
| UPD | Update Date | 1 |
| MP | Melting Point | 1 |

This substance also occurs in Reaction Documents:

| Code | Name | Occurrence |
|---|---|---|
| RX | Reaction Documents | 1 |
| RXPRO | Substance is Reaction Product | 1 |

Melting Point:

| Value (MP) (Cel) | Solvent (.SOL) | Ref. |
|---|---|---|
| 164 - 166 | aq. ethanol | 1 |

Reference(s):

1. Pavia, Michael R.; Lobbestael, Sandra J.; Taylor, Charles P.; Hershenson, Fred M.; Miskell, David L., J.Med.Chem., CODEN: JMCMAR, 33(2), <1990>, 854-861; BABS-5500188

Reaction:
RX

| | |
|---|---|
| Reaction ID: | 1529274 |
| Reactant BRN: | 393196, 105782 |
| Reactant: | 4-phenoxy-phenyl isocyanate, pyridin-4-ylamine |
| Product BRN: | 3560216 |
| Product: | 1-(4-phenoxy-phenyl)-3-pyridin-4-yl-urea |
| No. of Reaction Details: | 1 |

Reaction Details:
RX

| | |
|---|---|
| Reaction RID: | 1529274.1 |
| Reaction Classification: | Preparation |
| Yield: | 66 percent (BRN=3560216) |
| Solvent: | tetrahydrofuran |

Reference(s):

1. Pavia, Michael R.; Lobbestael, Sandra J.; Taylor, Charles P.; Hershenson, Fred M.; Miskell, David L., J.Med.Chem., CODEN: JMCMAR, 33(2), <1990>, 854-861; BABS-5500188